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Original Communications

THE CYANOSIS IN MITRAL STENOSIS

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IN THE beginning of the last century Corvisart[1] pointed out as a sign of heart affection a particular alteration of the face, characterized by a "violet coloration." A few years afterward, Bertin[2] expressed in a more precise manner the significance of this facial characteristic noted by Corvisart, referring to it as a sign of "induration and constriction of the heart valves." Subsequently, Bouillaud,[3] considering endocarditis and especially the symptoms and the diagnosis of the organic lesions of the valves with stenosis of the heart openings, referred to the facial changes in heart disease and reported a case of mitral stenosis in which there was this particular cyanotic tincture of the face.

Later, Huchard[4] differentiated, among the diverse clinical pictures of mitral stenosis, the cyanotic form that is characterized by a pronounced violaceous coloration of the face and lips which appears with the least effort and without considerable manifestations of cardiac insufficiency.

Barié,[5] considering the different types of facies in the valvular cardiopathies, differentiated the "aortic facies" of dull white color similar to that seen in anemia and the mitral facies of a violaceous coloration, the lips and wings of the nose being livid-cyanotic and the cheek bones crossed by bluish venules. On this cyanotic ground one can perceive a light subicteric tint that is more pronounced in the conjunctivae.

This particular cyanotic coloration which represents and distinguishes mitral stenosis has been explained by Walshe[6] as a result of interference with the oxygenation of the blood in the lung, brought on by the circulatory hindrance arising from a mitral lesion which obstructs the outflow of blood from the lung. Dautrebande, Fetter, and Meakins,[7] on the other hand, on the basis of a study of blood gases in four patients with mitral stenosis without clinical signs of lung congestion, have claimed that the saturation of oxygen of the arterial blood was normal, but, as soon as the

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TABLE

MEASUREMENTS MADE ON 22

CASE	DEGREE OF CYANOSIS	CIRCULATION TIME (SECONDS)*	VENOUS PRESSURE (MM. H_2O)	VITAL CAPACITY (LITERS)	ALVEOLAR AIR				ARTERIAL BLOOD GASES CONTENT (VOL. PER CENT)		VENOUS BLOOD GASES CONTENT (VOL. PER CENT)		ARTERIOVENOUS OXYGEN DIFFERENCE (VOL. PER CENT)
					OXYGEN		CARBON DIOXIDE						
					PER CENT	MM. Hg	PER CENT	MM. Hg	OXYGEN	CARBON DIOXIDE	OXYGEN	CARBON DIOXIDE	
1	+++	S = 50 R = 60	---	---	----	-----	---	----	14.7	39.7	6.8	43.4	7.9
	+++	---	---	1.40	15.87	113.91	4.65	33.37	16.9	51.1	9.9	56.9	7.0
2	++	R = 45	170	1.30	14.28	102.53	4.49	32.23	21.4	42.3	11.2	50.6	10.2
	+	S = 35 R = 40	164	2.05	13.07	93.38	4.75	33.93	24.0	40.5	10.9	51.0	13.1
3	+	---	---	2.00	15.22	108.06	5.27	37.41	23.6	45.0	8.0	55.0	15.6
	+++	S = 45 R = 48	250	1.50	15.74	112.38	4.47	31.91	23.3	40.1	8.0	53.1	15.3
	+	S = 35 R = 38	250	2.00	15.62	112.30	5.00	35.95	23.2	39.1	8.2	52.3	15.0
4	+	S = 50 R = 42	220	2.90	17.90	128.34	2.64	18.92	23.3	31.6	8.7	41.8	14.6
	0	---	140	3.10	15.11	107.43	4.71	33.48	19.7	40.6	13.4	53.2	6.3
	++	32(D)	240	---	----	-----	---	----	23.18	39.78	9.62	54.57	13.5
5	+	S = 24 R = 28	---	3.25	14.00	99.82	6.03	42.99	22.93	49.72	13.59	53.66	9.3
	+	S = 17 R = 25	238	---	----	-----	---	----	23.90	47.20	12.0	58.0	11.9
6	+	S = 30 R = 35	170	1.70	14.32	101.95	5.10	36.31	18.7	47.0	9.2	52.5	9.5
	0	S = 24 R = 26	117	2.30	14.17	101.03	5.20	37.07	19.6	43.7	10.8	51.5	8.8
7	+	S = 20 R = 35	183	2.20	15.86	113.24	4.65	33.20	19.0	38.0	6.0	48.0	13.0
8	++	S = 28 R = 32	205	2.10	16.05	114.75	3.61	25.81	16.9	36.0	7.0	48.0	9.9
9	+	R = 23	---	3.00	13.65	97.46	5.19	37.05	19.5	39.7	12.1	48.3	7.4
10	+	S = 24 R = 27	250	3.90	14.30	101.15	5.79	40.37	23.3	37.5	8.5	53.7	14.8
11	+	---	---	2.80	16.10	113.92	3.48	24.62	20.5	28.4	8.0	42.3	12.5
12	0	R = 35	205	2.30	15.72	111.76	4.14	29.43	19.1	39.0	11.9	45.0	7.2
13	+	S = 23 R = 28	---	2.45	14.04	99.68	4.79	34.00	16.1	51.9	9.0	57.4	7.1
14	++	---	250	2.20	15.58	112.33	3.73	26.89	26.18	42.9	----	---	---
15	0	---	115	3.50	13.14	94.08	6.06	42.38	17.5	53.0	8.45	58.0	9.05
16	+	S = 23 R = 25	85?	2.40	14.46	102.52	5.61	39.77	27.50	48.21	10.25	60.39	17.25
	++	---	95?	1.90	14.86	106.10	4.75	33.91	17.0	42.4	7.7	51.4	9.3
17	+	---	230	2.95	----	-----	4.26	30.33	24.6	33.8	9.3	50.0	15.3
	++	S = 35 R = 40	230	2.60	15.62	111.21	4.66	32.87	20.7	43.1	6.7	52.0	14.0
18	+	32(D)	240	---	----	-----	---	----	22.15	39.58	15.0	43.64	7.15
19	+	12(D)	122	---	----	-----	---	----	23.35	35.43	14.28	41.60	9.07
20	+	---	---	---	----	-----	---	----	19.11	45.18	8.95	51.13	10.55
21	++	25(D)	250	---	----	-----	---	----	21.75	45.98	11.16	50.43	10.59
22	+	---	---	---	----	-----	---	----	19.06	40.22	14.54	41.92	4.52

*S = taste and R = redness (histamine method); D = taste (decholin method).

I

SUBJECTS WITH MITRAL STENOSIS

OXYGEN CAPACITY (VOL. PER CENT)	OXYGEN UNSATURATION (VOL. PER CENT)		OXYGEN SATURATION (PER CENT)		CAPILLARY OXYGEN UNSATURATION (VOL. PER CENT)	REDUCED HEMOGLOBIN-CAPILLARY BLOOD (GM. PER CENT)	FUNCTIONAL CAPACITY	CLINICAL REMARKS
	ARTERIAL BLOOD	VENOUS BLOOD	ARTERIAL BLOOD	VENOUS BLOOD				
21.8	7.1	15.0	67.5	31.2	11.05	8.2	3	Mitral stenosis, auricular fibrillation. Congestive heart failure, pulmonary congestion
21.8	4.9	11.9	77.6	45.5	8.4	6.2	2 b	Improvement
27.1	5.7	15.9	79.0	41.4	10.8	8.0	2 b	Mitral stenosis, auricular fibrillation, pulmonary congestion
25.5	1.5	14.6	94.2	43.0	8.0	5.9	2 a	Improvement
24.8	1.2	16.8	96.0	33.0	9.0	6.7	1	Mitral stenosis, auricular fibrillation
24.8	1.5	16.8	94.0	34.3	9.15	6.8	2 b	Congestive heart failure
24.8	1.6	16.6	93.6	33.1	9.10	6.7	1	Definite improvement
24.0	0.70	15.3	97.1	36.3	8.0	5.9	3	Mitral stenosis, auricular fibrillation, congestive heart failure
20.7	1.0	7.3	95.0	64.7	4.15	3.0	1	Definite improvement
24.05	0.87	14.43	96.3	40.0	7.65	5.7	2 b	Congestive heart failure
26.48	4.55	12.89	86.6	51.4	8.72	6.5	2 a	Mitral stenosis, paroxysmal auricular fibrillation
26.30	2.40	14.90	91.0	46.0	8.65	6.4	1	Definite improvement
20.2	1.5	11.0	92.6	45.6	6.25	4.6	2 b	Mitral stenosis, auricular fibrillation
19.8	0.20	9.0	99.0	54.6	4.60	3.4	1	Definite improvement
20.0	1.0	14.0	95.0	30.0	7.5	5.5	1	Mitral stenosis, auricular fibrillation
20.0	3.1	13.0	84.5	35.0	8.05	6.0	2 b	Mitral stenosis, auricular flutter, pulmonary congestion
25.2	5.7	13.1	77.4	48.1	9.40	7.0	1	Mitral stenosis
28.0	4.7	19.5	83.3	30.4	12.10	9.0	1	Mitral stenosis, auricular fibrillation
22.4	1.9	14.4	91.8	35.8	8.15	6.0	2 b	Mitral stenosis, auricular fibrillation, adherent pericarditis
20.8	1.7	8.9	92.0	58.0	5.30	3.9	2 b	Mitral stenosis, aortic insufficiency
20.9	4.8	11.9	77.1	43.1	8.35	6.2	1	Mitral stenosis, auricular fibrillation
32.61	6.4	----	80.29	---	---	--	2 b	Mitral stenosis
18.8	1.3	10.3	93.6	45.0	5.80	4.3	1	Mitral stenosis, aortic stenosis
29.14	1.6	18.8	94.4	35.2	10.2	7.6	2 a	Mitral stenosis, aortic valve disease
24.5	7.5	16.8	69.4	31.5	12.1	9.0	3	Congestive heart failure, pulmonary congestion
27.7	3.1	18.4	89.0	34.0	10.7	7.9	1	Mitral stenosis, aortic valve disease, auricular fibrillation
27.7	7.0	21.0	74.8	24.2	14.0	10.4	3	Congestive heart failure, pulmonary congestion
22.56	0.41	7.56	98.18	66.48	3.98	2.9	1	Mitral stenosis, auricular fibrillation, "facies mitral"
23.77	0.42	9.49	98.2	60.0	4.95	3.6	2 a	Mitral stenosis, hyperthyroidism, auricular fibrillation, "facies mitral"
19.50	0.39	10.55	98.0	45.89	5.47	4.0	1	Mitral stenosis, "facies mitral"
22.52	0.77	11.36	96.5	49.55	6.06	4.5	1	Mitral stenosis, auricular fibrillation
19.66	0.60	5.12	96.9	73.90	2.86	2.1	2 a	Mitral stenosis, aortic insufficiency, "facies mitral"

venous pressure became increased and signs of visceral congestion appeared, arterial oxygen unsaturation set in. As the cyanosis of mitral stenosis is not well understood, it seems worth while to report studies on a group of patients.

METHOD AND MATERIAL

Each patient was investigated under basal conditions. The following measurements were made: The speed of the blood flow by the histamine[8] or by the decholin method;[9] the venous pressure by the direct method with a water manometer; the vital capacity of the lungs with the Verdin spirometer; the alveolar oxygen and carbon dioxide by the Haldane and Priestley method;[10] the oxygen and carbon dioxide content of the arterial and venous blood by the Van Slyke and Stadie method;[11] the arteriovenous oxygen difference; oxygen capacity of the blood; saturation percentage of the arterial and venous blood; reduced hemoglobin in capillary blood by the Lundsgaard and Van Slyke procedure;[12] estimation of the degree of cyanosis according to the method already described;[13] and functional capacity according to the point of view of the American Heart Association[14] (Table I).

Twenty-two patients were investigated. The distribution of the cases was as follows: Mitral stenosis with sinus rhythm, 3; mitral stenosis with auricular fibrillation, 14; mitral stenosis with aortic regurgitation and sinus rhythm, 4; mitral stenosis with aortic regurgitation and auricular fibrillation, 1. The clinical diagnosis as well as the state of the lungs was established by clinical, radiographic and electrocardiographic examinations. In 6 cases the diagnosis was confirmed by necropsy (Cases 1, 2, 4, 11, 16 and 17).

COMMENTS

Among the 22 patients studied only 2 (Cases 12 and 15) had no cyanosis, while the other 20 presented varying degrees of cyanosis. In the 2 patients without cyanosis mitral stenosis coexisted with aortic regurgitation, although there were patients with cyanosis with this same combination of valvular lesions (Cases 16 and 17, Table II).

Of the 20 patients with cyanosis (Table I), the reduced hemoglobin in the capillary blood was at least 4.5 gm. (which is the minimal quantity that is necessary for the appearance of the cyanotic coloration) in 15 (Cases 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 16, 17 and 21). In these 15 patients with cyanosis and increase of the reduced hemoglobin, the cause of the cyanosis varied. In 6 cases (Cases 3, 4, 6, 7, 11 and 21) it was peripheral cyanosis; that is to say, there was an increased delivery of oxygen at the capillaries. In the other 9 (Cases 1, 2, 5, 8, 9, 10, 13, 16 and 17) it was of the mixed variety, due to increased delivery of oxygen, on the one hand, and to increased arterial unsaturation, on the other. The latter was never found to be the only cause of cyanosis, that is to say, cyanosis was never exclusively of the central variety. In some of the patients with mixed cyanosis (Cases 2, 5, 16, and 17), when the cardiac failure diminished, the arterial unsaturation lessened or even disappeared (Cases 2 and 5), while with an increase of cardiac failure there was also an increase of the arterial unsaturation (Cases 16 and 17, Table II).

The greater peripheral utilization of oxygen, the cause of the cyanosis in the patients above mentioned, was due to circulatory stasis, which was partly a consequence of the existing cardiac failure (back pressure) and partly due to the venous hindrance in the region of the vena cava superior. This resulted from mechanical disturbances brought about by the enlargement of the left auricle and rotation of the heart due to stenosis of the mitral valve.

TABLE II

ARTERIAL OXYGEN SATURATION, CAPILLARY HEMOGLOBIN, AND DEGREE OF CYANOSIS IN 4 SUBJECTS WITH MITRAL STENOSIS WITH VARYING DEGREES OF FUNCTIONAL CAPACITY

CASES	DEGREE OF CYANOSIS	FUNCTIONAL CAPACITY	ARTERIAL OXYGEN SATURATION (PER CENT)	REDUCED HEMOGLOBIN IN CAPILLARY BLOOD (GM. PER CENT)	CLINICAL REMARKS
2	++	2b	79.0	8.0	Pulmonary congestion
	+	2a	94.0	5.9	----------
5	+	2a	86.6	6.5	----------
	+	1	91.0	6.4	----------
16	+	2a	94.4	7.6	----------
	++	3	69.4	9.0	Pulmonary congestion
17	+	1	89.0	7.9	----------
	++	3	74.8	10.4	Pulmonary congestion

This mechanical disturbance at the level of the vena cava superior in mitral stenosis has been observed by us over and over again when we performed catheterization of the right auricle, introducing a catheter through a vein of the fold of the elbow.[15] In normal people, as well as in patients with arterial hypertension or aortic regurgitation with varying degrees of heart failure, the catheter reached the right auricle without

TABLE III

VENOUS PRESSURE AND ARTERIOVENOUS OXYGEN DIFFERENCE IN 7 SUBJECTS WITH MITRAL STENOSIS WITHOUT HEART FAILURE

CASE	FUNCTIONAL CAPACITY	VENOUS PRESSURE (MM. H_2O)	ARTERIOVENOUS OXYGEN DIFFERENCE (VOL. PER CENT)
3	1	250	15.0
5	1	238	11.9
7	1	183	13.0
10	1	250	14.8
17	1	230	15.3
18	1	240	7.15
21	1	250	10.59

meeting any obstacle, taking the following course: vena axillaris and vena subclavia, the innominate vein and vena cava superior (Fig. 1). In the patients with mitral stenosis and enlargement of the left auricle, on the other hand, it was the rule that when the catheter reached the vena cava superior it met with an obstacle that prevented its arrival at the

right auricle; thus in more than one instance, in trying to overcome the obstacle by force and pushing the catheter with maintained pressure, its point turned around and entered the internal jugular vein (Fig. 2). The presence of this obstacle at the level of the vena cava superior may account satisfactorily for the increase of the venous pressure at the level of the elbow fold and the lack of correlation between pressure in the external jugular vein and the degree of heart failure in mitral stenosis, as was seen in the observations in Table III.

Increase of the arterial unsaturation as the cause of the central cyanosis in several of the cases studied cannot be attributed to a venous-

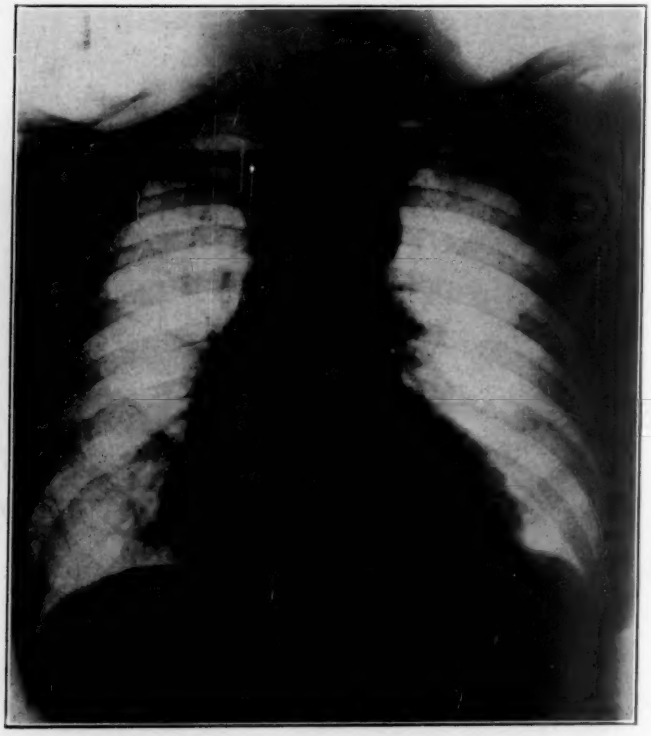

Fig. 1.—Radiogram showing the way followed by the catheter in arriving at the right auricle.

arterial shunt resulting from a congenital cardiac malformation or to a decrease of the tension of oxygen in the alveolar air, i.e., to alveolar hypoventilation.[16] It has to be related to pulmonary congestion, as suggested by Meakins and Davies,[17] and probably also to the alteration of the alveolar walls which Parker and Weiss[18] found in their histologic study of the lungs in cases of mitral stenosis. The stasis in the pulmonary circuit disturbs the gaseous interchange between the alveolar air and the blood flowing through the pulmonary capillaries, and in spite of the increase of the tension of the alveolar oxygen, as shown by analysis of the

alveolar air, the blood leaves the lungs with a higher degree of unsaturation of oxygen. Abatement of the heart failure decreases the pulmonary stasis and the saturation of the oxygen of the arterial blood increases, as occurred in Cases 2 and 5. In Cases 16 and 17 the arterial saturation diminished considerably with increase in the degree of the heart failure, and the cyanosis was mixed (Table II).

There remains to explain the light cyanosis of the cheeks and lips, i.e., the mitral facies in Cases 18, 19, 20, and 22, in which the blood that was

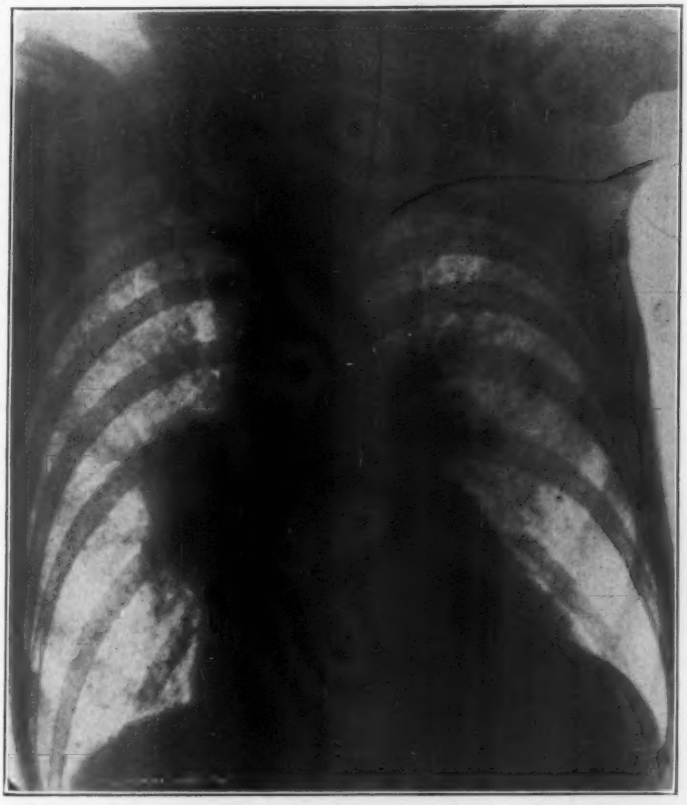

Fig. 2.—Radiogram showing the catheter turned around and entered by retrograde way in the internal jugular vein in a patient with mitral stenosis.

extracted from the vein of the elbow fold and from the radial artery did not show the existence of the minimal quantity of reduced hemoglobin which is necessary for the development of cyanotic coloration (Table IV).

As Harrison[19] has claimed, and Goldschmidt and Light[20] have shown, there may be cyanosis in heart failure by the mere dilatation of the venous capillaries. The predominance of the venous capillaries in the capillary net is the reason that the blood which is contained in them determines the coloration of the skin. As a result of this, the skin appears cyanotic even when, according to the estimate of Lundsgaard and Van

Slyke, the quantity of the reduced hemoglobin in the capillary net does not exceed minimum values.

The degree of heart failure (back pressure) and the obstacle at the level of the vena cava superior produced by the enlargement of the left auricle in mitral stenosis are held responsible for the blood stasis in the venous system and its consequence, namely, the dilatation of the venules

TABLE IV

ARTERIAL OXYGEN SATURATION AND FUNCTIONAL CAPACITY OF 4 PATIENTS WITH MITRAL STENOSIS AND "FACIES MITRAL," AND WITH REDUCED CAPILLARY HEMOGLOBIN UNDER "CYANOSIS THRESHOLD"

CASE	FUNCTIONAL CAPACITY	ARTERIAL OXYGEN SATURATION (PER CENT)	REDUCED HEMOGLOBIN CAPILLARY BLOOD (GM. PER CENT)	CYANOSIS
18	1	98.18	2.9	"Facies mitral." Nail cyanosis (+).
19	2a	98.2	3.6	"Facies mitral." Nail cyanosis (+).
20	1	98.8	4.0	"Facies mitral."
22	2a	96.9	2.1	"Facies mitral."

and venous capillaries of the face which causes the cyanotic coloration of the cheeks, chin, and lips (mitral facies), for which no increase of the reduced capillary hemoglobin is needed.

SUMMARY AND CONCLUSIONS

A study of the blood gases, alveolar air, venous pressure, and other aspects of the circulation was carried out in 22 cases of mitral stenosis, in 20 of which there were varying degrees of cyanosis. The cyanosis was due in 6 cases to a greater peripheral utilization of oxygen (peripheral cyanosis), and in 10 cases to increased peripheral utilization in the capillary net and to the increase of the oxygen unsaturation of the arterial blood (mixed cyanosis); in 4 cases the data obtained did not explain the cyanosis.

The dilatation of the small veins in the capillary net was brought on either by the venous hypertension of heart failure (back pressure), or by the increased pressure caused by an obstacle at the superior vena cava level, the presence of which was shown by catheterization of the heart; the latter may be the sole cause of the mitral facies.

We wish to express our gratitude to Professor Houssay for having allowed us to make some of the measurements of blood gases in the Department of Physiology, and to Dr. Soma Weiss for suggestions in the preparation of the manuscript.

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CORONARY ARTERY DISEASE ANALYZED POST MORTEM

With Special Reference to the Influence of Economic Status and Sex

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CORONARY artery disease as a cause of disability and death has been observed to occur with greater frequency among the economically well-to-do classes. This observation has been based largely on clinical impressions and, insofar as we are aware, has not been adequately substantiated by post-mortem findings. It was for this reason that in the course of an extensive study of coronary artery disease post mortem a special investigation was undertaken.

Studies relevant to the post-mortem incidence and degree of coronary atherosclerosis have been relatively few in number,[1, 2, 3, 4] and were made primarily to determine the influence of age, sex, and, in one instance, of race. No attempt was made, however, to note the apparent influence of "economic status" on the general incidence and distribution of the coronary artery disease.

To help in the solution of this problem, we have examined the post-mortem records of the Massachusetts General Hospital. They include a considerable number of cases from private departments (Phillips House and Baker Memorial) representing economically well-to-do patients, for comparison with cases from the public wards representing economically less fortunate members of society. We have determined the incidence and degree of significant coronary artery disease occurring in these two groups in order to test the accuracy of our clinical opinion.

It should be mentioned, however, that the patients now treated in the general wards of the Massachusetts General Hospital are not representative of the usual ward population seen in large city hospitals, or even representative of its own ward population of twenty years ago. From an economic point of view one would say that they come largely from the low middle class of wage earners, many of whom are able to pay in part for their hospitalization.

Through the courtesy of Dr. Tracy B. Mallory, we studied 3,400 consecutive post-mortem records of the Massachusetts General Hospital, dated from February, 1925, to September, 1937.* A careful examination

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*During this period 3800 post-mortem examinations were made, but because of certain restrictions the heart was either not examined or by superficial palpation only, in 400 instances. Prior to February, 1925, the description of the macroscopic appearance of the coronary arteries was not always sufficiently complete to be of value in the present analysis.

of the coronary arteries and their larger branches had been recorded in each instance, along with a detailed account of the macroscopic lesions.

TABLE I

INCIDENCE AND DEGREE OF CORONARY ATHEROSCLEROSIS

3,400 Consecutive Post-Mortem Cases

AGE GROUP	TOTAL CASES	CORONARY ATHEROSCLEROSIS			
		CASES	NARROWING		
			WITHOUT OCCLUSION	WITH OCCLUSION	TOTAL
0- 20	502	5 (1.0%)	0	0	0
21- 40	575	104 (18.0%)	8 (7.8%)	7 (6.7%)	15 (14.5%)
41- 60	1,271	656 (51.7%)	162 (24.9%)	80 (12.8%)	242 (37.7%)
61- 80	990	805 (81.3%)	300 (37.2%)	109 (13.3%)	409 (50.5%)
81-100	62	59 (95.0%)	33 (56.0%)	7 (11.9%)	40 (67.9%)
Total	3,400	1629	503	203	706

POST-MORTEM DATA

As shown in Table I, the 3,400 cases were divided on the basis of age into five groups of twenty years each. For the purpose of our analysis this appeared to be a relatively simple arrangement which emphasizes the three age periods (21 to 80) of greatest clinical importance. The possibility of error in estimating the degree of coronary artery narrowing is necessarily large. In order to minimize this possibility in our comparisons, we included only cases exhibiting definite narrowing or actual occlusion of the coronary arteries which we termed "significant coronary artery disease."

Sex Relationship.—The clinically observed disproportion between the incidence of coronary artery disease in men and women is amply supported by our studies. The disproportion was greatest in young adults, the men outnumbering the women approximately three to one, with regard both to significant coronary disease and to complete occlusion. In the middle age group the disproportion was less, especially as regards uncomplicated narrowing, in respect to which our figures indicated no significant difference. In instances of occlusion, however, the men still outnumbered the women two to one. A finding of considerable interest in the study was that at the age of 70 years, and over, there was no significant sex difference in the occurrence of coronary changes.

It seems, then, that insofar as sex is concerned the factor or factors responsible for the sex disproportion in coronary atherosclerosis are most effective in young adults, less significant in those of middle age, and of little or no importance in old age. Thus, if the male survives the hazards of coronary disease in youth and middle age he is on a par with the female in this respect in old age.

Economic Status.—The presence in this series of 600 patients from the private departments of the hospital offered an opportunity for special comparative study of this important group. A large number of post-mortem examinations is necessary for the establishment of reliable generalizations; those included here will serve as a nucleus for further comparison. It is essential to examine the data in relation to the age and sex of the individual groups. Furthermore, due to the extreme rarity of significant coronary artery disease prior to the age of 20 years, and its great frequency after the age of 80 years, only those patients

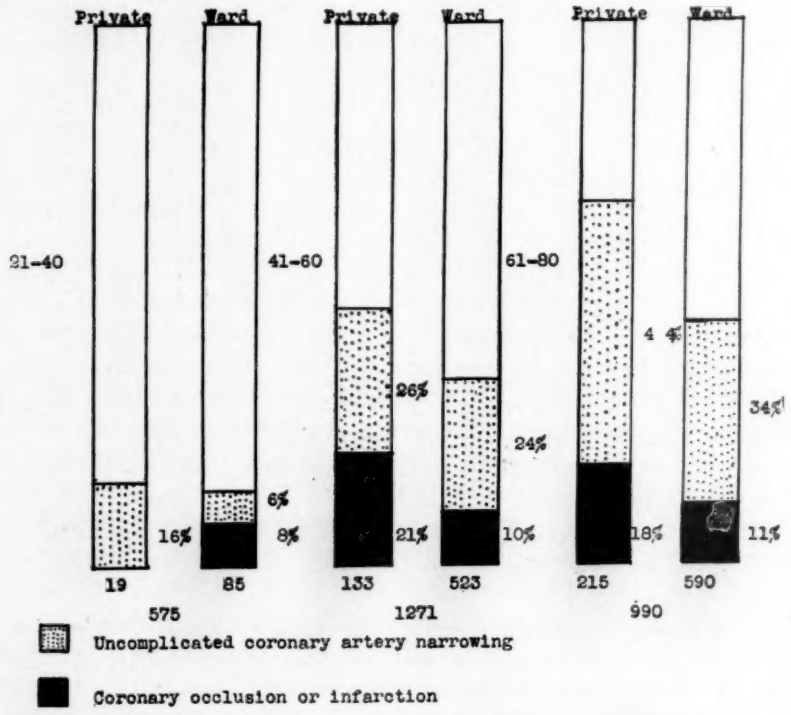

Fig. 1.—A comparison of the incidence and degree of coronary atherosclerosis on the basis of economic status.

whose age at time of death fell between 20 and 80 were included for this special study in relation to economic status.

Certain questions of a statistical nature arose when an attempt was made to analyze the material in detail. For example, it was necessary to determine whether the reasons for hospitalization and cause of death in the two groups were comparable. Also, in the course of tabulation and comparison, the number of cases occurring in certain groups was necessarily small, making it difficult to evaluate their significance. However, after making surveys of samples chosen at random from the total series, and after making computations for the determination of signif-

icance, Mr. Herbert Marks of the Statistical Bureau of the Metropolitan Life Insurance Company stated that the reason for hospitalization and the cause of death in the two groups were comparable, and that the number of patients in the groups used in the study was sufficient to serve as a basis for statistical conclusion.

The general level of coronary atherosclerosis in the private patients in all age groups was consistently greater than in those from the general wards. Furthermore, the incidence of coronary artery narrowing and occlusion follows this general trend.

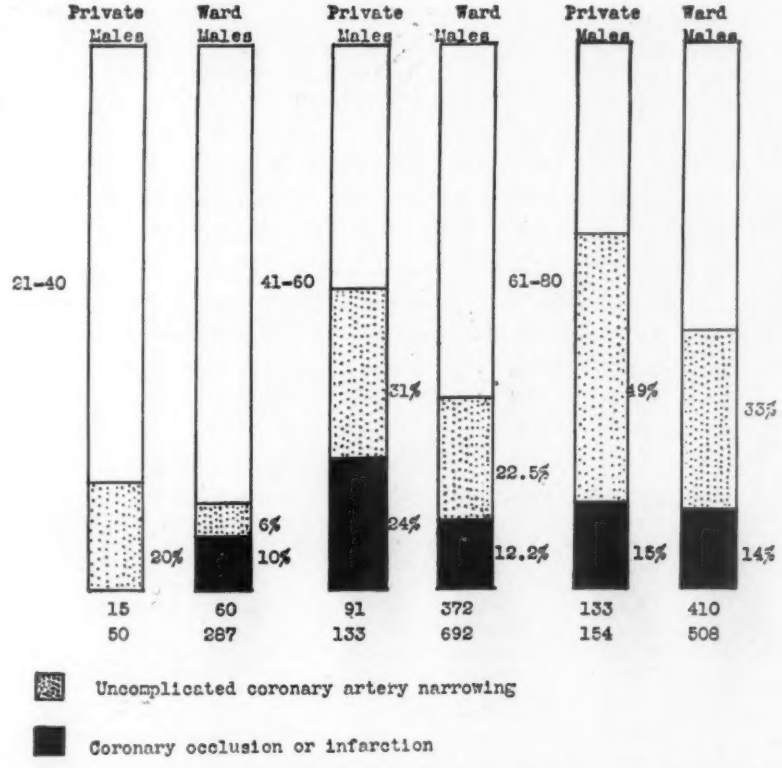

Fig. 2.—A comparison of the incidence and degree of coronary atherosclerosis in males on the basis of economic status.

In the young adults between 21 and 40 years of age the presence of seven instances of occlusion in the ward group in contrast to none in the private group is of some interest and suggests the need of further study. In spite of this finding, the incidence of recognizable narrowing of the vessels remained higher in the private patients of this age.

The most striking difference, however, between the two economic groups is reflected in the incidence of coronary occlusion in those between 41 and 60 years of age. The incidence in the private group was twice as great as in the ward group. This is a significant difference,

since the total number of post-mortem examinations in both groups for this age is considerable. The continued predominance of coronary occlusion in the private patients in the next group (between 61 and 80 years of age), although somewhat less striking, is still significant.

A further comparison of the two economic groups as regards sex necessarily reduces the number in certain instances to a level which rendered conclusions unreliable. It was justifiable, therefore, to compare only the male patients of the two groups. The greatest differences occurred in the middle age groups, in which coronary occlusion was twice as prevalent among the private patients as among those in the ward (Fig. 2).

CONCLUSIONS

In a study of the records of 3,400 consecutive post-mortem examinations made at the Massachusetts General Hospital between February, 1925, and September, 1937, the following facts were ascertained:

1. After the age of 70 years there was no difference in the incidence of coronary artery disease in men and women. Before that age there was much more in men than in women.

2. The relative incidence and the degree of coronary atherosclerosis were found to be significantly greater in the 600 patients from the private departments than in the 2,800 patients from the general wards. The greatest difference occurred in the middle-aged patients, in whom coronary occlusion was found to be twice as frequent in the private group. This difference was most striking in the middle-aged males. These findings are in general agreement with clinical impressions.

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THE ISOLATION OF NICOTINE FROM HUMAN URINE*

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NICOTINE usually elevates arterial blood pressure in man when it is absorbed in sufficient amounts from tobacco smoke. When it is injected into cats or dogs it causes powerful vasoconstriction and rise of arterial pressure. Since it is absorbed in large quantities daily by countless people, it is a matter of importance to ascertain its fate in the body. We have examined urine for its presence.

EXPERIMENTAL

Method of Extracting Pressor Substance From Urine.—Urine was collected from normal persons. It was made alkaline with sodium hydroxide (1 to 2 gm. of sodium hydroxide per liter) and extracted with ether in continuous extractors (two-liter capacity) for twenty-four hours. The ether extract was transferred to separatory funnels, washed with distilled water, and extracted three times with 0.1 N hydrochloric acid (about one liter of acid for a forty-eight-hour urine specimen).

The hydrochloric acid extract was reduced to small volume by means of vacuum distillation, transferred to a small beaker, and evaporated to dryness on a steam bath to remove the last traces of hydrochloric acid. The dry residue was taken up in 0.9 per cent sodium chloride solution, adjusted to neutrality with one N sodium bicarbonate solution, and made up to a standard volume of 6 c.c. From 0.1 to 1 c.c. of this extract was used for the assay.

In addition, pressor extracts were prepared by extraction of alkaline urine with benzene instead of ether. Active extracts were also obtained by adsorption and elution from animal charcoal by the technique described by Bain.[1]

Methods of Preparing Animals.—Arterial pressure was measured in cats weighing 2 to 3 kg. by inserting a cannula into a carotid artery and connecting it to a mercury manometer, using heparin as anticoagulant. The remaining carotid artery was ligated; both vagi were cut and a tracheal cannula was inserted for artificial respiration. The cat was now decerebrated on the Sherrington guillotine. Some animals were pithed after decerebration and others were pithed without being decerebrated. A pithed cat anesthetized with pentobarbital (33 mg. per kg. intraperitoneally) was found to be most satisfactory for assay of the pressor effect of urine extracts. The material to be tested was injected into a femoral vein.

A few experiments were carried out on dogs prepared in a similar manner, using paraldehyde (1.7 c.c. per kg.) as the anesthetic.

Pressor Effects of Extracts of Urine and of Oxalates and Picrates Prepared from These Extracts.—Numerous extracts of pooled urine specimens which were collected from normal men were prepared. Extracts made by ether extraction gave most uniform effects on the blood pressure of pithed cats (Fig. 1*A*).

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Solutions of crystalline derivatives (oxalate and picrate) of the pressor principle prepared from large quantities of normal urine produced an elevation of arterial pressure similar to that obtained from crude urine extracts. Comparable injections into the same animal revealed that the crystalline derivatives from urine extract were approximately as active as nicotine (Fig. 2). The supernatant fluid after removal of oxalate or picrate crystals produced no rise in arterial pressure. Likewise, solutions of sodium oxalate or picrate were found to have no pressor effect.

Comparing portions of the same extract, there was no difference in the height of the blood pressure rise produced in cats under ethyl urethane (subcutaneously), paraldehyde (orally), ether (inhalation), or pentobarbital (intraperitoneally) anesthesia. Greater rises in arterial pressure were produced in cats which were either decerebrated or pithed than in the intact animal, but there was no appreciable difference between decerebrated and pithed animals.

When 8 mg. of cocaine were previously injected as a sensitizing agent, the rise in blood pressure produced by the same dose of urine extract was neither augmented nor inhibited, although this amount of cocaine doubled the response to adrenin and partially inhibited the action of tyramine. The pressor effect of urine extracts was not reversed to depressor by previous injection of ergotoxine. The urine extract differed from adrenin and tyramine in that when injections were rapidly repeated (at intervals of less than fifteen minutes) the animals soon became refractory. About forty minutes were required to restore the original degree of reactivity.

Bilateral adrenalectomy did not alter the responsiveness of pithed cats to the action of urine extracts (Fig. 1*A*).

Other Pharmacologic Properties.—Contractions of the nictitating membrane were regularly produced by injection of extracts which simultaneously produced a marked rise of arterial pressure. Greater contractions of the nictitating membrane were obtained with tyramine than with urine extracts, although the rise in arterial pressure was less. Large doses of extracts (1 to 2 c.c.), when given to intact or decerebrated animals, often produced twitchings of voluntary muscle, vomiting, defecation, convulsions, and death.

Comparative Study of Individual Forty-Eight-Hour Urine Specimens.—Extracts of forty-eight-hour urine specimens obtained from a group of twenty-two normal men were tested several times on different cats and the average rise of blood pressure produced by 0.5 c.c. of each extract was calculated. Some of these extracts were also tested on dogs. The dogs were given 2.0 c.c. of extracts from nonsmokers and 0.2 c.c. of extracts from those who smoked. (All extracts were prepared so that 6 c.c. of the extract were equivalent to the total forty-eight-hour urine

specimens.) Much larger rises in blood pressure were produced by extracts obtained from the men who smoked than from those who indulged occasionally or not at all (Table I).

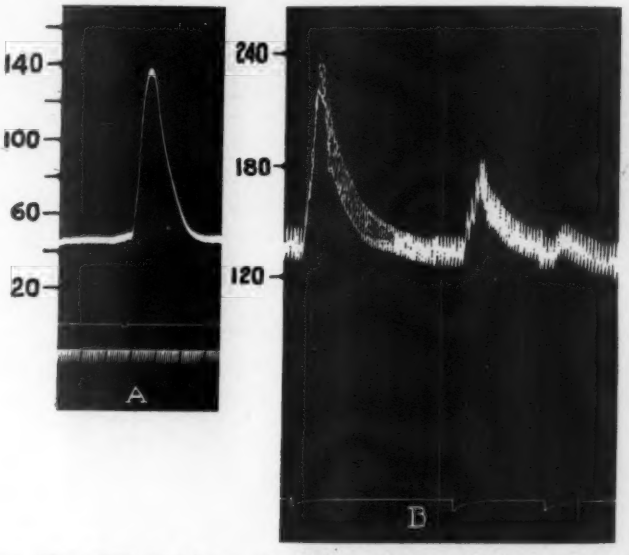

Fig. 1.—*A*, The effect of 0.8 mg. of nicotine picrate crystals prepared from pooled normal urine given intravenously to an adrenalectomized pithed cat under pentobarbital anesthesia. *B*, The effect of intravenous injection in a dog under paraldehyde anesthesia with vagi cut of (1) 0.3 c.c. of urine extract from period in which forty cigarettes were used, (2) 0.3 c.c. of urine extract from first twenty-four hours in which no tobacco was used, and (3) 0.3 c.c. of urine extract from the second twenty-four-hour period after smoking had been stopped.

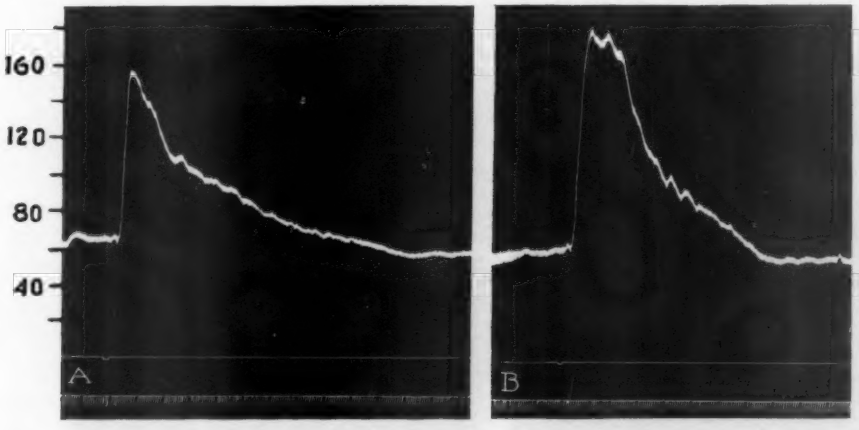

Fig. 2.—The effect of (*A*) the intravenous injection of 1.2 mg. of nicotine picrate crystals from pooled normal urine into pithed cat under pentobarbital anesthesia, and of (*B*) the intravenous injection given forty minutes later of 1.2 mg. of nicotine.

The effect of stopping the use of tobacco on the amount of nicotine extracted from the urine was demonstrated by withholding cigarettes for a forty-eight-hour period from one subject who regularly smoked

forty cigarettes a day, and collecting twenty-four-hour urine specimens during this period. In the same dog, a much smaller rise in blood pressure was produced by extracts of urine collected during nonsmoking periods than by the extract of urine collected when the subject was smoking his usual number of cigarettes (see Fig. 1*B*).

TABLE I

THE EFFECT OF INJECTION OF URINE EXTRACT ON BLOOD PRESSURE OF PITHED CATS AND INTACT DOGS

	AMOUNT OF TOBACCO USED PER 24 HOURS	AVERAGE RISE IN BLOOD PRESSURE (MM. HG)	NUMBER OF EXTRACTS TESTED
Cats:			
Nonsmokers or occasional smokers (0.5 c.c. of extract given)	Occasional cigarette	21	11
	Occasional pipe	37	4
	Total abstinence	33	3
	Total abstinence	35	3
	Total abstinence	38	3
	Total abstinence	34	1
	Total abstinence	11	1
	Total abstinence	4	2
Smokers (0.5 c.c. of extract given)	40-50 cigarettes	270	5
	40-50 cigarettes	183	2
	40 cigarettes	250	4
	40 cigarettes	190	2
	30 cigarettes	210	6
	30 cigarettes	131	3
	30 cigarettes	93	4
	20 cigarettes	135	5
	20 cigarettes	156	1
	20 cigarettes	112	2
	20 cigarettes	100	1
	20 cigarettes	73	2
	20 cigarettes	30	2
	4-5 cigars + pipe	134	1
Dogs:			
Nonsmokers or occasional smokers (2.0 c.c. of extract given)	None	6	1
	None	8	1
	None	4	1
	None	10	1
	None	8	1
	None	2	1
	None	4	1
	None	10	1
	None	8	1
	None	10	1
Smokers (0.2 c.c. of extract given)	40 cigarettes	30	1
	50 cigarettes	24	1
	50 cigarettes	38	1
	4 cigars + pipe frequently	33	1

Isolation and Identification of Nicotine from Normal Urine.—The urine was made alkaline with sodium hydroxide and extracted in a continuous ether extractor of large capacity (20 liters). The ether extract was washed with distilled water in a separatory funnel and extracted three times with 0.1 N hydrochloric acid. The hydrochloric acid extract was concentrated to a small volume by vacuum distillation. It was made alkaline by sodium hydroxide in the cold. The alkaline extract was steam-distilled until the distillate no longer gave a precipitate with silicotungstic acid. The distillate was extracted in a separatory funnel with ether until the

aqueous phase no longer gave a precipitate with silicotungstic acid. The combined ether extracts were dried with anhydrous sodium sulfate and filtered through paper. A solution of anhydrous oxalic acid in anhydrous ether was then added to the clear, colorless solution until precipitation was complete. The solution was allowed to stand in the icebox overnight.

The oxalate was dissolved in a small quantity of warm absolute alcohol and allowed to stand in the icebox for twenty-four to forty-eight hours. A crystalline oxalate deposited which had only a slight pressor activity. A further precipitate could be obtained by the addition of dry acetone. This oxalate was strongly pressor. A sticky residue was obtained on evaporation of the mother liquors which also had strong pressor properties. The oxalates failed to give sharp melting points, hence they were converted into picrates. The oxalates precipitated by acetone and the one recovered by evaporation were dissolved in water, made alkaline with sodium hydroxide, and again subjected to steam distillation. The distillate was transferred to a separatory funnel and extracted with ether. The ether solution was dried with anhydrous sodium sulfate and filtered. Alcoholic solution of picric acid was added and the precipitate recrystallized from warm alcohol. A light yellow crystalline picrate was obtained. The following data showed that it was nicotine picrate.

Nicotine picrate prepared from nicotine melted at 215 to 216.5° (uncorrected). A mixture of picrate prepared from urine (2.5 mg.) and nicotine picrate (2.5 mg.) melted at 215 to 216° (uncorrected). The results of analysis of the urine picrate are given in Table II.

TABLE II

	PICRATE FROM URINE (%)	CALCULATED FOR NICOTINE PICRATE (%)
C =	42.64	42.57
H =	3.18	3.25
N =	18.00	18.06

DISCUSSION

It has been shown that nicotine can be isolated in crystalline form as oxalate or picrate from the urine of human beings who smoke tobacco.* The pharmacologic properties of the substance isolated from urine are identical with those of pure nicotine. If tobacco smoking is discontinued, nicotine almost disappears from the urine within three to four days.

It has been known for many years that the injection of urine or extracts of it into anesthetized animals often produces a rise in arterial pressure. This has formed the basis of much speculation concerning the association of urinary pressor substances with the genesis of hypertension. Extracts of urine have been studied by several investigators,[1, 2, 3] but it is not always possible to ascertain from the description of the method of preparation whether the pressor substance was nicotine. In some cases it probably was.

It is understandable why much confusion exists concerning the results of urine examination for pressor substance from patients with hyper-

*Extracts of blood which appear to contain nicotine have also been prepared.

tension. In some, smoking was probably strictly interdicted, as for example, during hospitalization, while in others, as a result of confinement and emotional disturbance, indulgence was greater. Since the substance responsible for a large part of the pressor activity of urine extracts is nicotine, the relation of pressor activity to the condition of the patient would depend chiefly on whether tobacco was being used.

Little is known of the metabolism of nicotine. Biebl, Essex, and Mann[4] showed in heart-lung preparations from dogs that the ability of liver to destroy nicotine was greater than an equivalent mass of hind limb, and that the action of a comparable dose of nicotine on the blood pressure of a dog was much more pronounced after hepatectomy than before. It has been suggested that nicotine might be excreted in urine, but the evidence for it has rested chiefly on the observation that extracts of urine or organs cause contraction of leech muscle.[5, 6] Perez[7] has attempted to determine nicotine in urine by silicotungstic acid. It is difficult to say how successful he was because there appears to be no record of the amount he could recover by his method or how much was pure nicotine. He has shown wide variation in the nicotine content of various tobaccos, and suggested that nicotine might be retained in the body when renal function was reduced.

SUMMARY

1. Nicotine has been isolated as crystalline oxalate and picrate from the urine of persons who smoke. Its pharmacologic properties are the same as those of pure nicotine.

2. Most of the nicotine disappears from the urine within three to four days after smoking has been discontinued.

3. Nicotine appears to be the substance responsible for the marked pressor action of many urine specimens. Unless tobacco has been eliminated as a source of pressor substance in urine, conclusions relating urinary pressor substances to arterial disease may not justifiably be drawn.

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TISSUE PRESSURE: AN OBJECTIVE METHOD OF FOLLOWING SKIN CHANGES IN SCLERODERMA

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THERE has been no satisfactory objective method of estimating the effect of therapeutic procedures on the skin changes in scleroderma. We believe that the estimation of tissue pressure may be used in this way. The hardened and slowly contracting skin would be expected to have a direct effect upon the tissue pressure, particularly in the extremities where pressure is brought to bear upon the encased tissues from all sides. While making observations on this pressure in the subcutaneous tissue in patients with vascular disease, we found elevated values in scleroderma,[1] indicating that changes in tissue pressure might be used as an index of the progress of the disease. The present study was undertaken to evaluate this relationship.

The method has been described elsewhere.[2] It consists (Fig. 1) essentially of a U-tube water manometer (*a*) which is connected by rubber tubing (*b*) to a rubber pressure bulb (*c*) controlled by a screw clamp (*d*) and also connected to a 1.0 mm. bore glass adapter (*e*) to which is fastened a 27-gauge needle (*f*). Parallel lines, etched at millimeter intervals in the wall of the adapter, facilitate reading of slight movement of the meniscus. The beveled end of the needle was occluded with solder and four openings symmetrically drilled into the lumen through the wall of its distal third. In use, sterile normal saline was drawn into the needle and about half the way up the adapter, and the pressure in the system brought to atmospheric. The needle was then inserted into the subcutaneous tissues of the part to be studied. The pressure in the system was slowly raised by the screw clamp until the meniscus in the adapter just began to move. This pressure was taken as the subcutaneous tissue pressure. Aseptic technique was used throughout.

We have previously reported the normal range of tissue pressure for the common edema sites.[2] The values are summarized in Table I. The maximum value in any site was found to be 54 mm. of water at heart level. Elevations in venous pressure were found to influence tissue pressure. The full effect of venous pressure was not immediate; for short periods of time the effect was slight, but when prolonged, as in congestive heart failure, the tissue pressure was greatly elevated. Indeed, in all types of increasing edema studied, the tissue pressure was invariably elevated. However, in receding edema, the values were lowered, at times even below normal, to return finally to a normal level.[2] Thus far, in the absence of edema or increased venous pressure we have not found an elevation in tissue pressure except in scleroderma. Other conditions may exist, for example, in an area in which there is increased intrinsic or extrinsic pressure.

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TABLE I

SUBCUTANEOUS TISSUE PRESSURE (MM. H_2O) AT HEART LEVEL IN TEN NORMAL SUBJECTS

	DORSUM OF HAND	VOLAR SURFACE OF FOREARM	PRETIBIAL AREA	DORSUM OF FOOT
Mean	17.9	23.6	37.1	30.8
Maximum	30.0	40.0	54.0	43.0
Minimum	8.0	11.0	18.0	15.0

In seven patients with scleroderma we have found the subcutaneous tissue pressure to be elevated in the affected areas. The values varied from 338 to 26 mm. of water, the initial readings in these seven patients being 280, 234, 136, 76, 74, 34, and 28. Comparison of the mean values

TABLE II

TISSUE PRESSURE IN SEVEN PATIENTS WITH SCLERODERMA (MM. H_2O)

NO.	AGE AND SEX	SITE	REMARKS						
1	21 F	Right forearm	4/22/37 280	4/23/37 Right cervical Sympathec.	4/28/37 Edema 338	5/ 4/37 Parathyroidectomy	6/17/37 216	8/24/37 128	5/31/38 112
2	40 F	Right forearm Left forearm	8/24/37 234 50	8/25/37 Left cervical Sympathec.	9/30/37 Mild edema 68	11/11/37 240 320 76			
3	9 F	Left pretibial	7/ 8/37 74	7/15/37 Left lumbar Sympathec.	11/ 9/37 180	3/18/38 134	5/13/38 108		
4	52 M	Dorsum Right hand Dorsum Left hand	2/16/38 28 26	2/17/38 Thyroid extract started	4/11/38 34 26				
5	29 M	Dorsum Right hand	76						
6	48 M	Dorsum Right hand	136						
7	42 F	Dorsum Right hand Dorsum Left hand	12/18/37 34 28	5/30/38 26 38					

with the normal is illustrated in Fig. 2. The values not only varied from patient to patient but also from region to region in the same patient, depending upon the degree of the process (Table II). For

example, in one patient (No. 2), with areas of calcification and with localized patches in which the sclerodermatous process was more marked than in the surrounding skin, the tissue pressure varied considerably. In one of these thickened areas in the right forearm the tissue pressure was found to be 320 mm. of water, while in a less involved nearby area the value was 240. In the opposite, less severely involved arm, the value was found to be 76 mm. of water. It appeared, therefore, that the tissue pressure varied with the degree of involvement.

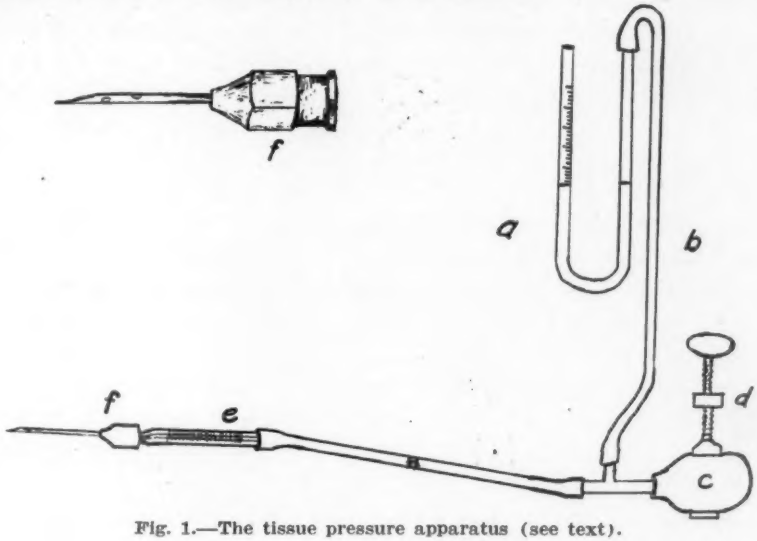

Fig. 1.—The tissue pressure apparatus (see text).

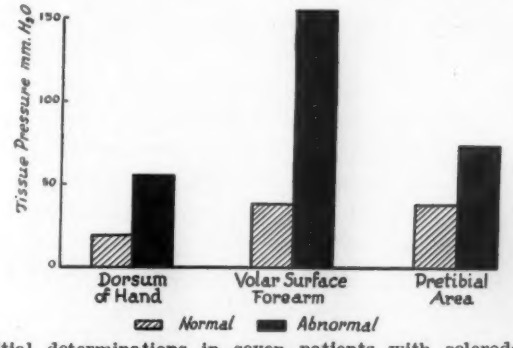

Fig. 2.—Mean initial determinations in seven patients with scleroderma, compared with mean normal values.

A similar relationship was found from patient to patient. In patients No. 4 and 7, with early changes, tissue pressure was found to be within the upper limits of normal, while in patient No. 5, with more marked involvement, the value was distinctly elevated. Again, in patient No. 6, with a still more marked process, the pressure was found to be even higher.

Not only does tissue pressure serve as an objective method for determining the degree of the sclerodermatous process, but it may also

serve as a method for quantitatively measuring the degree of change in the involved area from time to time, with or without the influence of therapeutic measures. In a typical patient (No. 1), followed for thirteen months, distinct changes were noted in the subcutaneous tissue pressure. The value in the dorsum of the right forearm, which was markedly involved, was 280 mm. of water. Five days later, following a right stellate ganglionectomy, the value rose to 338 mm. of water. At this time the patient had edema of the entire right arm. A parathyroidectomy was performed eleven days later. Six days following this operation, the tissue pressure was found to be 216 mm. of water, and nine weeks later it had dropped to 128 mm. of water. Clinically, as well, the patient had improved. All determinations were made in the same area. That the procedure may also follow the increased severity of the disease is exemplified by patients No. 2 and 3 in whom, in spite of therapeutic procedures, the initial values of 50 and 74 mm. of water increased to 76 and 180 mm. of water, respectively.

Patients have not yet been followed sufficiently long to evaluate the merits of various therapeutic procedures, and the present report is limited to a demonstration that measurement of tissue pressure may be used as an objective method of following these changes. A detailed report of results and an evaluation of therapeutic procedures, together with other physiologic observations, will be published at a later date in collaboration with the Department of Surgery.

COMMENT

There is much indirect evidence[3] to indicate that the contracting skin of scleroderma increases the pressure on the underlying structures. The appearance of the skin and the pathologic changes in the underlying structures have long indicated this possibility (Fig. 3). As early as 1898, Osler[4] described the patient as "encased in an ever shrinking, slowly contracting skin of steel." The skin is stretched and smooth, with obliteration of the ridges and sulci. As Mayo and Adson[5] state, the changes, such as cyanosis, swelling, pain, atrophy, contraction, deformities, and disuse, simulate those that arise from a plaster cast that is too tight. The skin is pale, particularly over the prominences when the hand is flexed. Furthermore, it has been noted,[3] and this was well shown in one of our patients, that extension of the fingers resulted in ischemia of the finger pad, an indication of the tightness of the skin. Further indirect evidence of the increased pressure on the underlying tissue is the disturbance in circulation. Skin temperature and pulsatile phenomena are diminshed in the involved areas, apparently as a result of the increased pressure upon the blood vessel walls. Our direct determinations of the subcutaneous tissue pressure substantiate this belief. As far as we know, this is the first time that increased pressure in the subcutaneous structures has actually been directly demonstrated in this

disease. Since the phenomena accompanying the increased pressure appear to parallel the severity of the disease, we have available now a direct method whereby we may not only follow the general course of the disease, but also the variations in the severity of the process in different areas. It is obvious that a rise in tissue pressure may occur before the process is manifest clinically. Under such circumstances tissue pressure determinations may lead to a diagnosis of sclerodermatous changes before the disease may be recognized in that patient or in a particular area by other methods.

It is well known that vascular changes may precede the development of scleroderma and also that such changes may be secondary to the sclerodermatous process. Our results give direct evidence upon a mechanism of the latter type. With tissue pressures of the magnitude which we have found, which have exceeded the normal venular and capillary

A. *B.*

Fig. 3.—Section of normal skin (*A*) and sclerodermatous skin (*B*), showing the differences in quality and quantity of dermal structures.

pressures, one would expect a collapse of these vessels. Permanent collapse would be prevented by a building up of the venular and capillary pressures from the arteriolar side, provided no collateral circulation were possible. It is conceivable that in a localized area, if the process were severe, and if a collateral circulation were adequate, a rise in tissue pressure, exceeding the venous pressure and the pressure of the adjoining tissues, could result in localized ischemia and atrophy. Proximal to the involved areas in which the tissue pressure exceeds the normal venous pressure, the venous pressure would fall to its usual normal value. This is exemplified by the conditions existing when a pneumatic cuff about the upper arm is inflated to a value exceeding the normal venous pressure and less than diastolic blood pressure. In such an instance the venous pressure distal to the cuff will build up and equal the cuff pressure to re-establish the circulation, while the venous pres-

sure proximal to the cuff is unaffected. As a routine measure, venous pressure measurements are difficult in these patients because of the character of the skin and the small size of the veins in the involved areas. Fortunately, however, a small vein was accidentally entered while taking the tissue pressure in the dorsum of the arm in one of our patients. The venous pressure in this vein at heart level was 228 mm. of water, while the pressure at heart level in the uninvolved anticubital space was 86 mm. of water. Such direct venous pressure determinations made with the tissue pressure apparatus are extremely accurate, as we have shown elsewhere.[6]

Such an interrelationship of tissue pressure and intravascular pressure would demand that a rational approach to the treatment of scleroderma include measures which tend to reduce the tissue pressure in these subjects. We are at present engaged in studying certain aspects of this problem.

SUMMARY AND CONCLUSIONS

1. The determination of tissue pressure may be used as an objective method for evaluating changes in the skin of patients with scleroderma.

2. The subcutaneous tissue pressure at heart level in the involved areas in seven patients with scleroderma was found to vary from 26 to 320 mm. of water in the absence of edema. In normal individuals comparable determinations have never exceeded 54 mm. of water.

3. The effect of the increased tissue pressure of scleroderma upon the contained blood vessels has been discussed.

4. Since the subcutaneous tissue pressure can be objectively determined and recorded by this method, and since this pressure has been found to vary with the severity of the sclerodermatous process, it offers promise as a guide to the effectiveness of therapeutic procedures. The method also offers a diagnostic aid in patients suspected of scleroderma when clinical findings are minimal and before subjective symptoms have become prominent.

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THE POSTPHLEBITIC VARICOSE ULCER

Surgical Treatment With Special Reference to the Communicating Veins of the Lower Leg*

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IN GENERAL there are two types of ulceration of the lower leg associated with varicose veins. This was pointed out originally by Homans,[1] in 1917. The first type is the simple varicose ulcer which is found in association with a varicose and incompetent condition of the long or short saphenous veins. They are readily healed by the obliteration of the varicose veins by multiple injections of a sclerosing solution into the involved veins, or better by high ligation of the long or short saphenous veins in addition to the injections. The second type, the postphlebitic varicose ulcer, is the ulceration which may develop on the lower leg from one to twenty years after a thrombophlebitis that has involved the deep veins of the leg. In contradistinction to the simple varicose ulcer, this type is characterized by its chronicity and the difficulty of obtaining a cure. The long or short saphenous veins or both of them are usually found incompetent in the postphlebitic leg. In addition, some or all of the communicating veins of the leg which connect the deep system of veins with the superficial ones are found to be incompetent. Thus, if the Trendelenburg test is carried out it will be found that the superficial veins of the lower leg fill rapidly from the deep veins through the communicating veins as well as from superficial ones. It is felt that the incompetence of the communicating veins explains the difference between these two types of ulcers.

An antecedent history of deep phlebitis cannot be elicited in all patients with this type of ulceration. However, in most cases one gets a history that at some time previous to the appearance of the ulcer the patient developed a swollen leg following pregnancy, an operation, a serious illness, or severe trauma to the extremity. The appearance of the ulceration and the skin surrounding it is very characteristic. Frequently the actual ulceration will be only a few centimeters in diameter, although in long-standing cases it may completely encircle the leg. When the patient seeks medical treatment the ulcer is covered with a dirty exudate from which a variety of organisms may be cultured. Sometimes hemolytic streptococci are present, but as a rule they are not. The skin about the ulcer for a distance of 5 to 10 cm. presents a purplish cyanotic hue when the leg is in a dependent position. A dark brownish pigmentation

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of the skin is seen in cases of long-standing ulceration. The more central portion of the skin frequently has an edematous, hypertrophied appearance. After removal of a dressing over the ulcer it is not uncommon to observe many droplets of clear, amber-colored fluid form on the discolored skin. On palpation of the leg it is found that there is a brawny edema of the subcutaneous tissues which may encircle the leg from the level of the malleolus to just below the knee. More commonly the edema is localized to the inner aspect of the lower leg. There is usually a very sharp line of demarcation between the normal and the edematous tissues. In many cases due to the edema, and in others to fibrous tissue beneath the skin, it may be impossible to see or palpate the varicose veins. Frequently they are felt as soft elastic channels running through the brawny and fibrous subcutaneous tissues.

The present forms of treatment of the postphlebitic varicose ulcer leave much to be desired. They may be divided into two types. The first are conservative procedures which may be termed "temporary healing measures." They consist in the use of elastic bandages,[2] paste boots and chemical applications such as gentian violet,[3, 4] balsam of Peru, pastes and ointments of various materials, the injection of sclerosing solutions into the varicose veins,[5] and the electrical method of iontophoresis with acetyl-beta-methylcholine chloride.[6] It would be an unusual year in which no new types of ointments or chemicals were described in the medical literature. The multiplicity of these remedies is sufficient evidence of the ineffectiveness of all of them.

The second type of treatment consists of surgical methods. These are chiefly the use of skin grafts either with or without excision of the ulcer. They have been described by Mayo,[7] Homans,[1] Trout,[8] Brown, et al.,[9] Pennoyer,[10] and Douglas.[11] The results by excision and skin grafting in our clinic have been gratifying in many cases, especially those done by Homans' technique. Nevertheless, there are a certain number of failures and recurrences. Because of the unsatisfactory results with both the conservative and surgical methods of treatment a careful analysis of the cause of these ulcers was made. As a result of this study a new form of treatment was developed.

The method that was devised is divided into five steps. The first one is the healing of the ulceration. This is accomplished by putting the patient to bed and elevating the affected leg on pillows so that it is at, or slightly above, the level of the heart. Warm compresses of a 2 to 4 per cent boric acid solution are applied to the ulcer area every two hours. If hemolytic streptococci are present, compresses of a surgical solution (Dakin's) of chlorinated soda are used. In some cases, when the ulcer is small, it will heal spontaneously under this regime. When the larger ulcerations become sufficiently clean, usually within one or two weeks, they are covered with Thiersch skin grafts. After ten days to two weeks the grafts will have taken solidly, and then the patient is ready for the

second step in the treatment. This consists in the ligation of the long saphenous vein of the affected limb at the saphenofemoral junction in the groin. If the ulcer is located on the posterolateral surface of the leg the short saphenous vein is ligated at the saphenopopliteal junction in the popliteal space. These operations are done under 1 per cent novocain infiltration anesthesia a few days before the patient is to be discharged from the hospital. It is important to ligate these veins at this time because it helps keep the ulcer from breaking open after the patient is allowed up. In addition, it is important to ligate them before operating on the communicating veins, because if the incision for the latter should become infected, there is then no danger of septic emboli being cast off into the circulation from the saphenous veins, as occurred in one of the patients reported in this series.

The third step consists in an ambulatory period of about six weeks. The treatment during this time is directed toward keeping the ulcer healed until the skin of the lower leg is sufficiently clean to permit ligation of the communicating veins of the lower leg without danger of infection developing in the operative wound. Skin grafts will rapidly disintegrate and the ulcer will soon recur if some support is not furnished to the lower leg. Accordingly, it was found that an elastic adhesive bandage applied directly to the skin from the toes to just below the knee provided excellent support in most cases. If a patient is sensitive to the adhesive compound on the bandage, an Unna's paste boot is applied instead. These forms of support should be changed every two weeks. In most cases it is possible by this means to prevent the recurrence of the ulcer and to get the skin in a condition for operation on the communicating veins within six weeks from the time the patient was discharged from the hospital.

The fourth step consists in the ligation of the communicating veins of the lower leg. These are a series of vessels which connect the deep and the superficial systems of veins. The former are the posterior tibial, anterior tibial, peroneal, and popliteal veins, and the latter are the long and short saphenous veins. Under normal conditions the communicating veins have valves which allow the blood to pass only from the superficial system to the deep system. The communicating veins of the lower leg have been divided into three main groups; the medial, the anterior, and the lateral (Figs. 1, 2, and 3). This was done in order to facilitate their surgical exposure. The medial group is made up of the posterior tibial and the medial subdivision of the anterior tibial communicating veins. They connect chiefly with the long saphenous system, and are found on the medial side of the lower leg posterior to the inner edge of the tibia. The anterior group consists of the central and lateral subdivisions of the anterior tibial communicating veins. They lie on the anterolateral surface of the lower leg between the tibia and fibula. They also join tributaries of the long saphenous vein. The lateral group is made up of

the communicating veins arising from the peroneal veins posterior to the fibula. They join with the short saphenous system. In addition, the popliteal communicating vein is included in this group. It is found posteriorly in the mid-lower leg. This vein may either join the short saphenous or tributaries of the long saphenous vein. In most patients

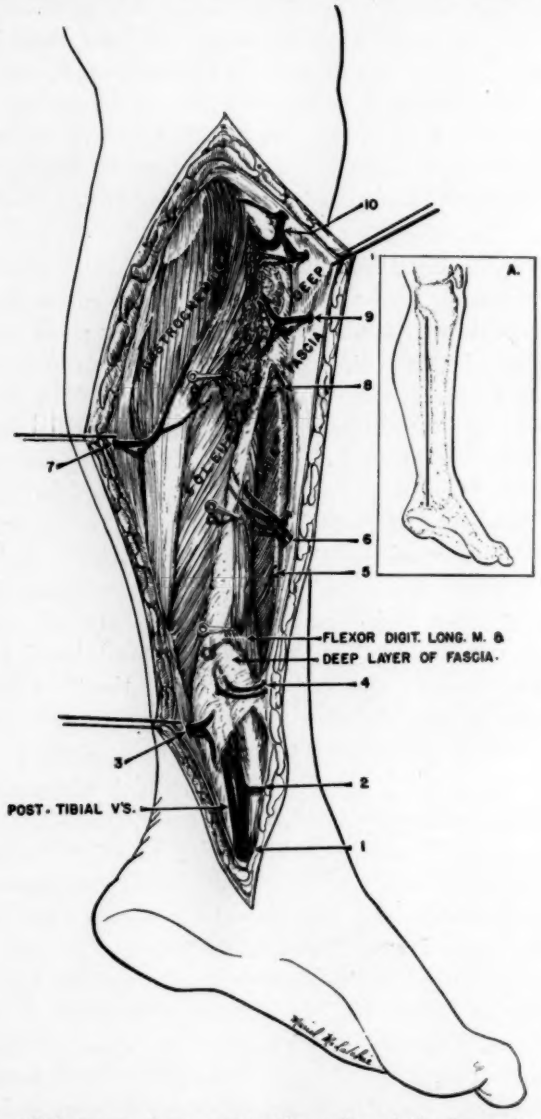

Fig. 1.—The medial group of communicating veins of the lower leg. A dissection of the medial aspect of the lower leg to show the medial group of communicating veins. The dissection has been carried out beneath the deep fascia. In the lower part of the leg the lamina profunda of the deep fascia has been divided to show the origin of the lower communicating veins. No. 1, 2, 3, 4, 6, 9, and 10 are posterior tibial communicating veins. No. 5 and 8 belong to the medial subdivision of the anterior tibial communicating veins. No. 7 represents a perforating vein which drains blood from the muscles through the deep fascia to the superficial veins. The inset shows the location of the incision used in the operation for the ligation of these veins. (From Ann. Surg. April, 1938.)

there are six to eight veins in each group, so that there is a total of twenty to twenty-four of them. For a more detailed account of these veins reference should be made to a recent article by Linton.[12]

After the patient is admitted for the ligation of the communicating veins the skin is very thoroughly cleansed before performing the operation. Since fungus infection of the skin is practically always present

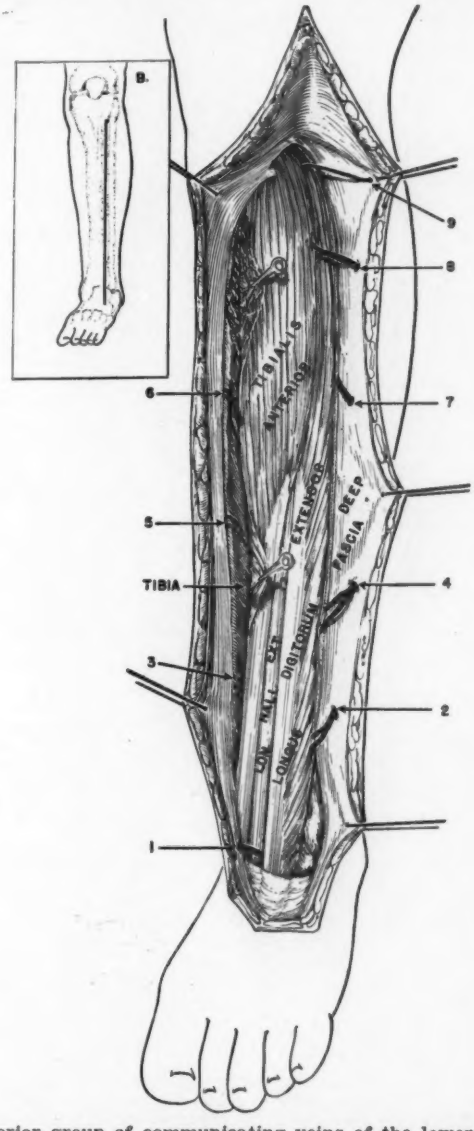

Fig. 2.—The anterior group of communicating veins of the lower leg. A dissection of the anterior aspect of the lower leg to show the anterior group of communicating veins beneath the deep fascia. No. 1, 2, 4, 7, 8, and 9 are the lateral subdivision of this group emerging along the anterior peroneal intermuscular septum. The tibialis anticus muscle is retracted laterally to show the veins of the central subdivision, No. 3, 5, and 6, on the lateral aspect of the tibia. The inset shows the location of the incision used in the operation for the ligation of these veins. (From Ann. Surg. April, 1938.)

about the old ulcer area, a fungicide is a great aid in cleaning it up.* One which has been found most efficacious consists of a 95 per cent ethyl alcohol solution containing 2 per cent resorcinol, benzoic acid, and boric acid. This is painted on once or twice a day after washing the leg with soap and water.

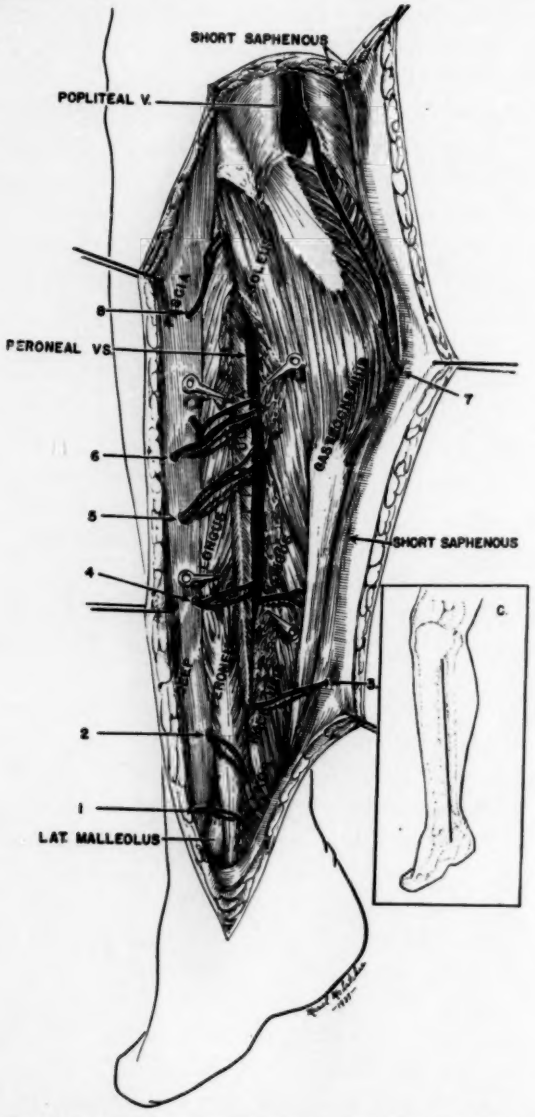

Fig. 3.—The lateral group of communicating veins. A dissection of the postero-lateral aspect of the lower leg to show the lateral communicating veins as they arise from the peroneal veins and pass outward along the posterior peroneal intermuscular septum. These are No. 1, 2, 3, 4, 5, 6, and 8. Posteriorly, the deep fascia has been elevated to show the popliteal communicating vein, No. 7. The short saphenous vein is shown superficial to the deep fascia. The inset shows the incision used in the operation for the ligation of these veins. (From Ann. Surg. April, 1938.)

*It is felt that fungus infection plays an important role in the etiology of varicose ulcers, and further work is in progress in an attempt to substantiate this view.

Ligation of the communicating veins is performed under spinal anesthesia. If the medial group is to be ligated the patient is placed in the Sims position with the affected extremity down. For the lateral group the patient lies face downward with the feet everted, and for the anterior group he lies on his back. The anatomic study of the veins revealed that they could all be readily exposed through three straight longitudinal incisions. The locations of these are shown in the insets of Figs. 1, 2, and 3. The use of straight incisions is especially emphasized. The incisions are carried through the deep fascia down to the muscles. The dissection is readily made between them and the deep fascia, as the only structures encountered are the communicating veins with small arteries accompanying them and a loose areolar connective tissue. They are divided and ligated beneath the deep fascia. The wound is carefully sutured with interrupted stitches in the fascia and the skin. Black silk (size No. 5) has been used in the majority of the cases in this series. The leg is placed in a posterior plaster shell from the toes to just below the knee. This immobilization aids primary healing. The dressing is done for the first time on the tenth postoperative day, when half of the skin stitches are removed. The remainder are taken out on the twelfth day. If the wound has healed per primam, postural leg exercises are commenced about the twelfth day to re-establish normal circulatory tone. These exercises are a modification of those described by Buerger[13] and Allen,[14] in that the period of elevation is longer than the period of dependency. They are done by elevating the legs to a thirty or forty degree angle with the horizontal for a period of three minutes. Then the lower legs are hung over the side of the bed for two minutes. This is followed by a five-minute rest with the legs in the horizontal position. The exercises are done in half-hour or hourly periods for a total of three or four hours a day. When the patient is allowed out of bed, the affected leg is bound firmly from the toes to the knee with an elastic adhesive bandage.

The fifth step in the cure of the ulceration consists in the postoperative care after the patient is discharged from the hospital. An elastic adhesive bandage or a paste boot is worn for a period of two to four weeks. Following this the patient should be instructed to wear an elastic stocking or a bender bandage for a period of several months to control the edema which is likely to develop. In addition, it has been found important that the patients bathe their legs and feet frequently with soap and warm water. After thoroughly drying the leg the ulcer area is painted with the fungicide that was used preoperatively. The purpose of this treatment is to eradicate the dermatitis, presumably of fungus origin, which so often persists following the operation. In some cases superficial ulcerations have developed postoperatively as a result of this dermatitis, but all of them have responded very rapidly to the above treatment.

Thirty cases of postphlebitic varicose ulcer in which the ulcer was treated by this method during 1937 at the Massachusetts General Hospital are reported in this paper. Twenty-three of the patients, or 77 per cent, were women, and seven, or 23 per cent, were men. The ages ranged from 22 to 66 years. Divided according to decades there were one in the third, ten in the fourth, nine in the fifth, seven in the sixth, and three in the seventh. These statistics point to the fact that this disease is much more common in women than in men and manifests itself chiefly in the middle age group, as 26, or 87 per cent, of the cases occurred between the ages of 30 and 60 years.

Fig. 4. Fig. 5.

Fig. 4.—A photograph of the medial side of the left lower leg of a colored woman aged 58 years showing a postoperative phlebitic ulcer of twenty years' duration. This had been open intermittently and treated with salves and elastic bandages.

Fig. 5.—A photograph of the same leg taken May 7, 1938, ten months after the ligation of the communicating veins. There was very marked fibrosis of the subcutaneous tissues in the lower one-half of the leg. The line of the incision is seen in the upper portion of the leg and behind the malleolus. It has disappeared in the region of the old ulcer area. The patient wears a bandage part of the time. There is slight edema of the entire leg. The fungicide mentioned in the paper has been used two to three times a week. The ulcer has remained healed during this time and the result is to be classed as excellent.

A definite history of a preceding attack of deep thrombophlebitis was obtained from twenty-three patients. In two cases the history was questionable and in five it was not obtainable. In fourteen cases the phlebitis occurred post partum, in six it developed during the course of an infectious disease, in two it was postoperative in nature, and in one it followed trauma to the leg. The phlebitis occurred from five to forty years

prior to the admission to the hospital. A blood Hinton test for syphilis was reported on twenty-six of the cases, in only one of which was it positive.

There were forty-one ulcers present in this group of thirty patients. Thirty-two, or 78 per cent, were located on the medial side of the leg, six, or 15 per cent, were on the posterolateral surface, and three, or 7 per cent, were on the anterolateral aspect. In nineteen cases the ulcers had been present for one to ten years. Eight had been present for ten to twenty-five years. The longest duration was forty years, and there were only two that had been present for less than one year. In twenty-three

Fig. 6.—A close-up photograph of the ulcer area in the same patient taken ten months after the ligation of the communicating veins. The whitish tissue represents the area of marked subcutaneous fibrosis. The incision is visible in the upper and lower portions of the photograph but not in the central part. The two irregular dark areas in the center of the photograph are the skin grafts placed over the ulcers twelve months before this photograph was taken. This was very soft and pliable, excellent evidence that the fibrosis in the subcutaneous tissues is not the cause of these ulcerations.

cases the lesion was unilateral and in the remaining seven it was bilateral, making a total of thirty-seven extremities operated upon.

Forty-five operations were done on the communicating veins of the lower leg. Some patients had several ulcers on one leg, necessitating operating on two or more groups of communicating veins. One patient had all three groups of veins on each leg ligated because of ulcers over the internal and external malleoli of both legs. The operations and operative mortality following ligation of the communicating veins for

forty-one postphlebitic varicose ulcers were as follows: Thirty-five, or 78 per cent, were performed on the medial group of veins; seven, or 15 per cent, on the lateral group; and three, or 7 per cent, on the anterior group. It is interesting to note that in thirty-five extremities, or 95 per cent of the thirty-seven affected legs, the medial group were ligated, indicating that these veins are the ones which most commonly become incompetent. There was one death in this group of patients, a mortality rate of 2 per cent. It was directly attributable to sepsis in the operative wound. This resulted from inadequate preoperative preparation of the skin of the lower leg, as the communicating veins were operated upon twelve days after the ulcer was skin-grafted. The rule now is not to ligate these veins until six weeks after the ulcer has healed. Another lesson learned from this case was that the saphenous veins should be ligated before the communicating veins, because the death was due to septic emboli arising from the saphenous vein which had not been ligated. Since then this vein is tied off before the patient is discharged from the hospital the first time. The operative mortality based on the number of operations on the communicating veins was slightly over 2 per cent.

TABLE I

END RESULTS

POSTPHLEBITIC VARICOSE ULCERS (1937)

Thirty-five Extremities (Twenty-eight Patients)*

NO. EXTREMITIES	PER-CENTAGE	DURATION FOLLOW-UP	RECURRENCES	PER-CENTAGE
17	49	1-1½ yr.	1	6
7	20	9-12 mo.	0	0
10	28	6- 9 mo.	0	0
1	3	5 mo.	0	0
			1	3

*One patient in the group of thirty died from postoperative infection and one other patient could not be traced.

Follow-up studies were made on twenty-eight of the twenty-nine patients who survived the operation (Table I). One patient could not be traced. In this group there were thirty-five extremities that were operated upon. In seventeen, or 49 per cent, the operation had been done one year, or more, before the follow-up examination; in seven, or 20 per cent, nine months, or more, before; in ten, or 28 per cent, six months, or more, before; and in one, or 3 per cent, five months before. Twenty-four patients were examined personally and the remaining four replied by letter to inquiries concerning their legs.

The results in all the cases except one were very satisfactory, as in only one case was there a recurrence of the ulceration. This was in a woman, operated on thirteen months previously, who suddenly developed, two weeks prior to the follow-up studies, an open lesion at the site of the old ulceration associated with an itchy vesicular rash. The original ulcer

had remained healed until that time. This result should not be classified as a failure, as the recurrent ulcer rapidly responded to ambulatory treatment with boric acid solution compresses and the fungicide mentioned above. In the remainder of the cases the results as far as the ulcerations were concerned could be classed as excellent. Thirty-nine ulcers, or 97.5 per cent of the forty that were present when the patients were first seen, were healed at the time of this follow-up study.

TABLE II

ANALYSIS OF END RESULTS

A. THIRTY-FIVE EXTREMITIES			B. FORTY ULCERS		
Elastic support all day	6	(17%)	Ulcers healed	39	(97.5%)
Elastic support part of day	7	(20%)	Ulcers not healed	1	(2.5%)
No support	19	(54%)			

In the majority of the patients the affected extremity, when only one was involved, still remained larger than the normal leg. This was due to varying amounts of a brawny type of edema, presumably the result of damage to the lymphatics at the time of the original deep thrombophlebitis. Bandages or elastic stockings were worn all day on six extremities, or 17 per cent, because of edema; on seven, or 20 per cent, they were only worn for varying periods during the day, for instance, for protection during working hours; on nineteen, or 54 per cent, no supporting bandages or stockings were worn. Information concerning the remaining extremities was not obtained.

DISCUSSION

The results obtained in the treatment of postphlebitic varicose ulcers by the method described indicate the importance of severing the communications between the deep and superficial veins when the valves in these communicating vessels are incompetent. It is worthy of note in these cases that it was necessary to inject very few of the superficial veins with a sclerosing solution following division of these vessels; in some cases no injections were needed. This indicates that the cure of the postphlebitic varicose ulcer depends in a great measure on preventing the hydrostatic pressure of the deep system of veins from being directly transmitted to the superficial veins.

The importance of the communicating (perforating) veins in the etiology of varicose ulcers has been recognized for many years. Homans,[1] in 1917, and Trout,[8] in 1929, stressed the role these vessels play in the etiology of the ulcer formation and recommended that they be ligated, but did not discuss the operative technique. In addition, an operation known as the "flap" operation for the ligation of the communicating (perforating) veins was done at the Massachusetts General Hospital for a number of years. The operation consisted in the raising of a flap of skin and fascia by means of a curved incision over the region where the

incompetent veins were present, or around a healed ulceration. The communicating veins were ligated beneath the deep fascia in the same way as is described in this paper. However, the operation fell into disrepute because (1) the curved incision not infrequently resulted in necrosis of the skin edge of the flap, which often required weeks or months to heal, and (2) the incision was usually a relatively short one so that the operation was frequently incomplete and recurrences resulted. Ligation of the communicating veins is therefore not an original or new operation. However, the entire operative procedure that is described in this paper for the treatment of postphlebitic varicose ulcers is original and is based on anatomic dissections.

The medial group of communicating veins was found most often to be incompetent. Of these the ones in the lower half of the leg were usually the most dilated. This apparently is because of the fact that the veins in this region pass out through tendinous structures which give little if any support to the veins, so that they may readily be stretched by increased venous pressure and so become incompetent. In the upper half of the leg they pass out between large muscle bellies which give them more adequate support. The anterior and lateral groups of communicating veins likewise have greater muscular support than the veins in the lower half of the inner side of the leg. These facts probably explain the greater frequency of medial ulceration—in this series 78 per cent.

In the postphlebitic leg with ulceration it is very difficult to palpate the communicating veins because of edema and fibrosis. However, the location of the ulcer indicates which group or groups of veins are incompetent. If the ulcer is situated on the medial or inner side of the leg it is the medial group of communicating veins that is incompetent; if it is on the anterolateral surface it is the anterior group, and if it is located on the posterior or posterolateral surface it is the lateral group. In some patients multiple ulcerations may be present so that two or more groups may be involved. An ulcer located over the anterior aspect of the tibia so that it extends on the anterolateral as well as the inner aspect of the leg usually indicates that the medial and anterior groups are incompetent. The long saphenous vein should be ligated at the saphenofemoral junction if the medial or anterior groups of communicating veins are to be ligated, and the short saphenous vein in the popliteal space if the lateral group is to be ligated.

The use of an efficient fungicide both in the preparation of the skin for operation and for use postoperatively is a very important adjunct to the surgical treatment that has been described.

CONCLUSIONS

1. A series of forty-one postphlebitic varicose ulcers in a group of thirty patients is reported.

2. A new method of treatment by ligation of the saphenous veins and the communicating veins of the lower leg is given.

3. Follow-up studies on these patients, made at intervals varying from five months to one and one-half years after treatment, are reported.

4. Thirty-nine, or 97.5 per cent, of the ulcerations were healed at the time of the follow-up study.

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INTRACRANIAL VASCULAR LESIONS*

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INTRACRANIAL vascular lesions comprise a very small but important group of lesions simulating tumor of the brain. They may be associated with vascular lesions elsewhere in the body; for example, thromboangiitis obliterans of the brain has been described as a clinical entity associated with generalized thromboangiitis obliterans. However, the intracranial vascular lesions which are not associated with vascular lesions elsewhere in the body create most of the difficulty in differential diagnosis.

At one time, it was thought that intracranial vascular lesions occur only among elderly people; however, congenital or developmental anomalies may occur among children and young adults. The blood vessels of the brain are subject to various types of malformation and anomalies from which symptoms may develop insidiously or suddenly. Rupture of a congenital aneurysm involving an artery leading into or arising from the circle of Willis may cause diffuse subarachnoid hemorrhage with sudden headache and collapse. The presence of such an aneurysm rarely is recognized until it has ruptured, although, once suspected, the diagnosis may be made before rupture occurs by means of roentgenograms of the head taken immediately after the injection of thorium dioxide (thorotrast) into the internal carotid artery. Arteriovenous aneurysms of the brain have been considered congenital in origin, although in other portions of the body such lesions are usually of traumatic origin. An arteriovenous aneurysm of the brain, according to Dandy,[1] consists of dilated arteries with an angiomatous formation interposed between the arterial supply and a tremendously dilated venous system into which arterial blood enters. Whereas it is true that some authorities state that arteriovenous aneurysms of the brain are always congenital, in a review of our cases it was found that in a certain number there was a definite history of injury preceding the development of symptoms. We may assume that in these cases there is an underlying congenital tendency, but the traumatic etiological factor must not be underestimated. To further this conception, Cushing and Bailey[2] quoted Schück,[3] who believed that whereas the vascular lesions may arise from a developmental fault, they are capable at a given time, owing to trauma or some other stimulus, of becoming active and producing symptoms.

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Intracranial vascular lesions have been divided into several classifications. Cushing and Bailey[2] seem to have divided them into the most simple and practical groups in their book "Blood Vessel Tumors of the Brain." These groups are telangiectasis, angioma venosum, arterial angioma or aneurysmal angioma. This classification includes only the vascular lesions over the surface of the brain. In addition to these, aneurysms of the carotids and anterior, middle, and posterior cerebral arteries produce symptoms of supratentorial tumor, and aneurysms of the vertebral, basilar, and cerebellar arteries simulate tumors of the cerebellopontine angle and cerebellum.

ANEURYSMAL ANGIOMAS

The presence of aneurysmal angioma may be suspected if a patient relates a long history of repeated convulsive seizures followed by temporary weakness or paralysis of one or more extremities. However, such a history also may be associated with tumors of the brain. Sometimes, roentgenologic examination of the head is of value and may give evidence of characteristic calcification in the walls of the abnormal blood vessels. Auscultation of the skull should be routine in the examination of all patients with intracranial lesions because the bruit, of which the patient may be unaware, often is detected with the stethoscope. Although a bruit may indicate the presence of a vascular lesion, we have encountered a number of cases in which bruits have been associated with increased intracranial pressure produced by a tumor of the brain.

The surgical treatment of aneurysmal angioma sometimes is followed by discouraging results. However, ligation of the artery with or without cauterization of the vein may relieve jacksonian convulsions, but there is always danger of producing permanent paralysis. Probably the most successful results are in cases in which the wormlike collection of vessels produces irritation of the cortex, and ligation and cauterization do not destroy the blood supply to the deep structures of the brain. Such a case was the following:

CASE 1.—A woman, aged 25 years, came to the clinic complaining of generalized convulsions, pain in the head, and visual difficulty. She had experienced occasional headaches for the previous four years, and sometimes she would become stuporous during the headaches and could be aroused only with difficulty. A generalized convulsion occurred the day before the delivery of her only child, one year before her examination at the clinic. The convulsion lasted a few minutes during which she bit her tongue. Following a normal delivery her general health was good until nine months later. While planting flowers in the garden she suddenly lost consciousness again and bit her tongue. She recovered and walked to the house following which she had a severe convulsion and was unconscious for four hours. One month previous to her registration at the clinic she had a sudden onset of sharp pain which was projected from the occiput around the base of the skull, was associated with vomiting for several hours, and was followed by unconsciousness lasting four or five days, for which she was hospitalized elsewhere. A week before her examination at the clinic she had an attack of numbness involving the entire left arm and hand which

lasted for several hours. She had experienced failure of vision for one month before examination at the clinic.

Neurological examination and roentgenologic examination of the head gave negative results. Examination of the eyes revealed a left homonymous upper quadrant hemianopsia. No bruit could be heard on auscultation of the head. Ventriculograms revealed a lesion in the right rolandic region. Craniotomy disclosed a normal appearing dura under increased tension, and when the dura was reflected a wormlike aneurysmal vascular lesion involving the sylvian and rolandic vessels was found (Fig. 1). The entire hemisphere pulsated. During the dissection of the dura from the arachnoid two large arteries were torn, necessitating ligation. Following recovery the patient was given one course of radiotherapy. Residual weakness of the left extremities did not occur. Four months following operation she had experi-

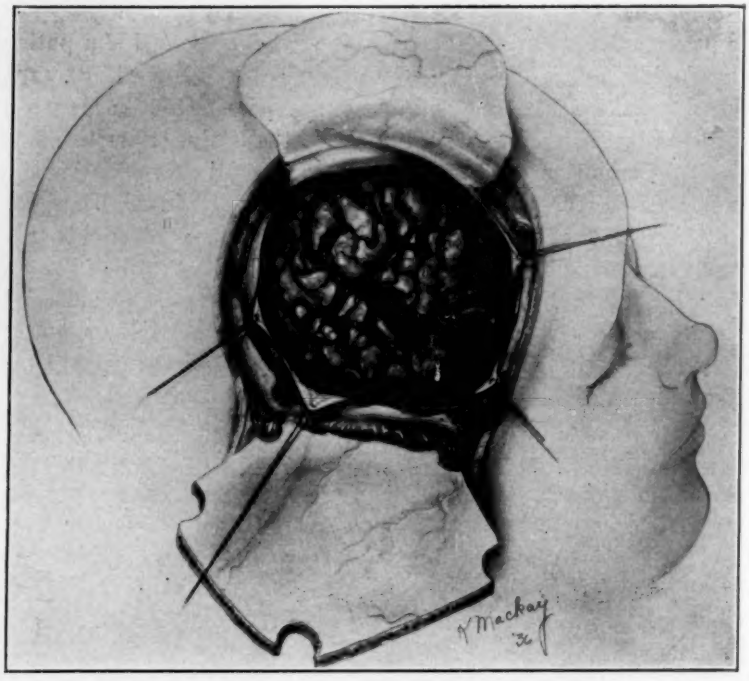

Fig. 1.—Aneurysmal vascular lesion producing convulsions, unconsciousness, and paresthesias.

enced neither headache nor attacks of jacksonian or generalized convulsions, although she was taking phenobarbital. Two years later, after a strenuous round of bridge and social activities, she had slight numbness of the left arm but otherwise had been perfectly well in the interval.

CASE 2.—A woman, aged 26 years, came to the clinic complaining of paresis of the left arm and generalized convulsions. At the age of 10 years she began having attacks of numbness and weakness of the left hand when she was under emotional excitement. At 18 years of age, one or two weeks before a menstrual period, she noticed a similar attack of numbness which lasted only a few moments. At the same time she began to have fainting spells. At the age of 22 years she was shocked by the death of her fiancé and, following this, she had spells of numbness of the left hand which became progressively more frequent and of longer duration.

After a sudden marriage and divorce she entered a nurses' training school and in the operating room became unconscious and had a generalized convulsion in which the left arm waved about and became spastic. She recovered in two or three minutes. After three such attacks she was sent home with a diagnosis of epilepsy. Following another convulsion she was sent to a hospital and after a week's observation she awoke at 3 o'clock one morning and noticed that her left arm was paralyzed. The paralysis disappeared in three hours. Later, the same morning, the arm became paralyzed again, and in addition she experienced numbness and weakness of the left leg. This disability persisted for four months, during which time there was slight recovery of motion of the hand and arm. During this time she had generalized and jacksonian convulsions every week or ten days.

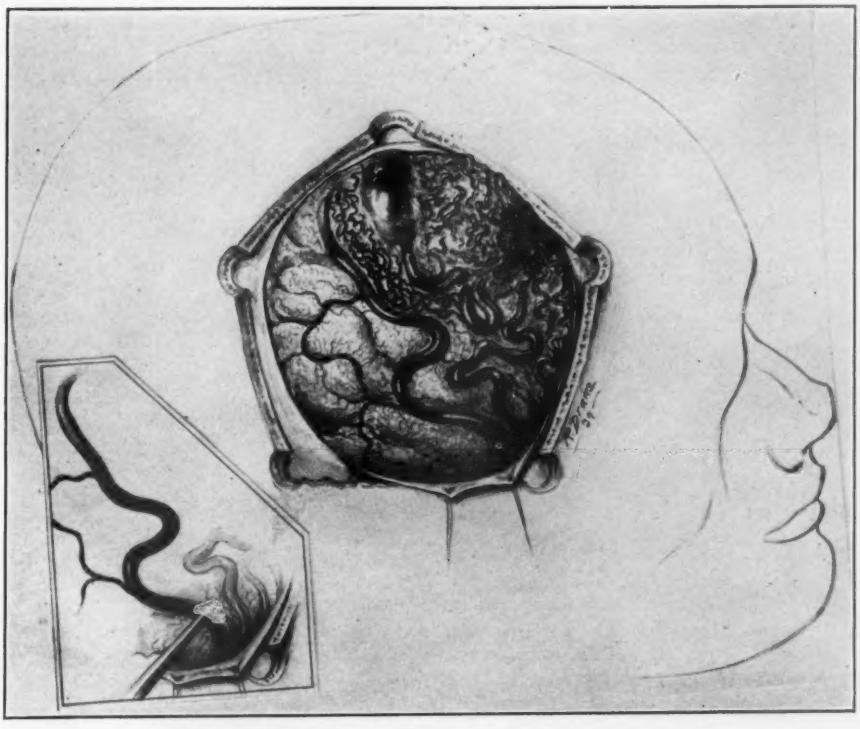

Fig. 2.—Aneurysmal angioma exposed at operation.

On general examination, considerable weakness, loss of tone and slowness of movement, and mild atrophy of the entire left upper extremity with an absence of reflexes were noted. Examination of the eyes and roentgenologic examination of the head gave negative results.

At operation, an aneurysmal angioma involving the right parietal region was found. Arterial blood could be seen coming from the middle cerebral artery, communicating through large vascular ramifications with communicating veins of the longitudinal sinus (Fig. 2). This mass measured about 7 cm. in diameter and 1 to 4 cm. in thickness. The entire parietal region of the brain had a bluish appearance and a definite arteriovenous lesion could be demonstrated by compressing the arterial branches of the middle cerebral artery. The larger arteries were ligated and the entire mass was coagulated, and as the coagulation of the vessels progressed there was definite shrinkage of the mass (Fig. 3).

Following operation, the sensation of the hand improved and she could move it more freely than before operation. She did not have difficulty in walking. A year later, although she was complaining of slight weakness in her left hand and arm, there had been neither grand mal seizures nor loss of consciousness, but there were occasional small convulsive seizures of the left hand. With the use of sedatives, phenobarbital, and bromides, she did not have further attacks.

Sometimes, merely decompression will help patients who have an aneurysmal varix, and it is very difficult at the time of operation to know when to employ conservative measures and when to be radical in treatment. A decompression followed by sedation may lead to gratifying results.

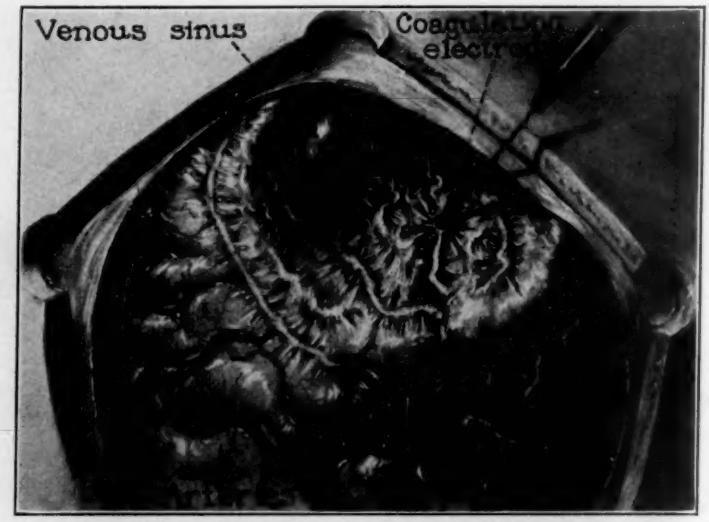

Fig. 3.—Aneurysmal angioma following ligation and coagulation.

CASE 3.—A man, aged 42 years, had been well until sixteen years before his examination at the clinic. While reaching for the telephone his right upper extremity became paralyzed, and this was associated with numbness and tingling. The paralysis gradually disappeared during the next three months, and except for an occasional transient attack of numbness of the right upper extremity, he was practically well for fourteen years. In the two years previous to registration at the clinic he had experienced an attack every week associated with minor cramplike contractions of the entire upper extremity. He had lost consciousness with about one-fourth of the attacks, which were initiated by cramping and drawing of the right hand and arm.

On examination it was found that 50 per cent of the strength in the entire upper extremity had been lost and that the reflexes were hyperactive. Craniotomy revealed a varicosity of the vessels, particularly the arteries, over the cortical region of the left hemisphere, involving particularly the arm center (Fig. 4). The vessels were greatly enlarged and were increased in number. Ligation and coagulation were not done, but a decompression was performed at the base of the flap. The patient returned home and was instructed to take a sedative, luminal. Two years later he was still having slight jacksonian convulsions involving the upper extremity about every month, but had not experienced generalized convulsions or attacks of numbness since the operation.

Sometimes there is definite evidence of trauma preceding the development of symptoms of intracranial lesions, and if an aneurysmal angioma is found at the time of operation, trauma must be considered one of the etiological factors. In some of these cases it is also possible to perform a palliative operation, ligating some vessels and coagulating others to reduce the severity of the attacks and make the patient more comfortable. However, if the lesion involves the motor or speech area it is sometimes better to withhold further surgical treatment.

CASE 4.—A man, aged 49 years, came to the clinic complaining of jacksonian convulsions involving the entire right side of the body. In the spring of 1918 he had struck his head against a dugout timber, the point of contact being the left parietal region. He was unconscious for a few moments, and vomited; he had headaches for twenty-four hours. Following this he returned to duty. Three years later the

Fig. 4.—Cortical aneurysmal varix.

right arm and leg became very tired on exertion. Seven years after the accident he noticed weakness of the right arm and leg which disappeared in a few days. The first convulsion occurred nine years after the accident. When examined six weeks after the first convulsion he complained of repeated twitching of the right side of the face followed by loss of consciousness. He was very confused on recovery. He was given phenobarbital for one year, during which time he had three attacks, two very slight and one severe, in which jacksonian convulsions of the right side of the face and body occurred and were followed by loss of consciousness. Subsequently, he had sixteen attacks; thirteen were jacksonian in type, involving the right side, and in three loss of consciousness occurred.

On examination, slight residual weakness of the right arm and leg were found. Roentgenologic examination of the head and examination of the eyes gave negative results. There was a diminution of reflexes of the right extremities and slight tenderness over the left parietal region of the head. The involvement predominantly of the right side indicated that the lesion was in the left hemisphere. The left parietal lobe was exposed at operation. The brain was under moderate tension and the precentral convolution in its midportion was covered by a mass of arteries

which were poorly defined but had the appearance of an angle worm 3 cm. in diameter. From the central portion of this mass the dilated vessels radiated and appeared to communicate directly with the branches from the middle cerebral artery. These vessels varied in size from 0.5 mm. to 3 or 4 mm. The normal arteries, which usually have the appearance of capillaries, were dilated and seemed to form this angiomatous mass. There was definite pulsation synchronous with the pulse. The situation of the mass in the left cerebral hemisphere and the slight degree of motor

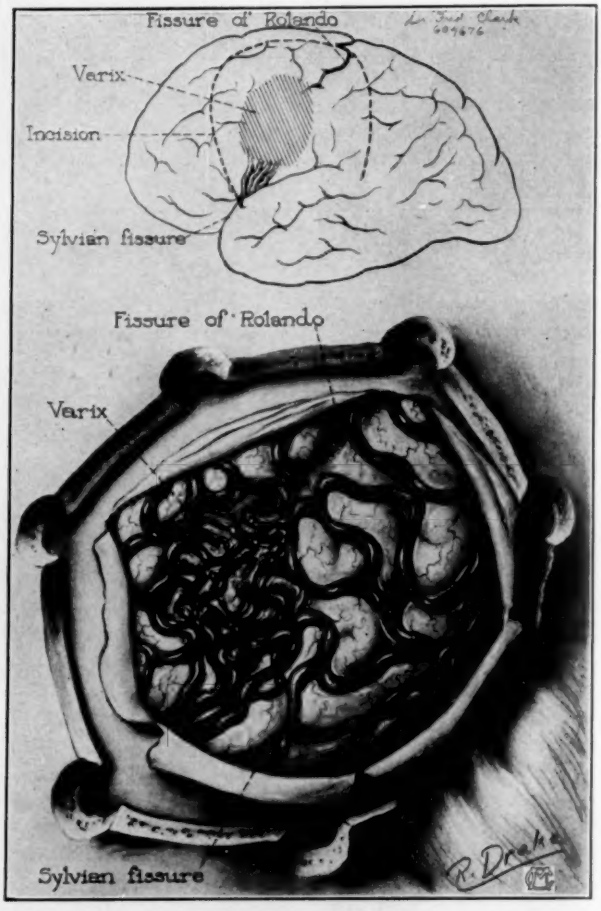

Fig. 5.—Aneurysmal angioma.

weakness on the right side contraindicated any radical surgical treatment (Fig. 5). Two days after operation the patient had a generalized convulsion. He was given phenobarbital for sedation, and four weeks after operation a very slight seizure involved the tongue. An intensive course of deep roentgenotherapy was given. He was examined four years after operation, with negative results. During the time that he had been taking three grains of luminal a day, he had been having about one attack in two months, consisting of twitching of the tongue with slight drawing of the right side of the face. Loss of consciousness had not occurred with any attack.

INTRACRANIAL ANEURYSMS

Intracranial aneurysms may be classed as arteriovenous or saccular in type. Saccular aneurysms may occur in any of the cerebral vessels and are most frequent in the region of the circle of Willis (Fig. 6). Saccular aneurysms of the intracranial portion of the internal carotid artery may be associated with different clinical pictures, depending on their size and situation. Supraclinoid aneurysms may simulate basofrontal tumors, with changes in the visual fields owing to pressure on the optic nerves or chiasm, anosmia, and mental aberration. By extension posteriorly they

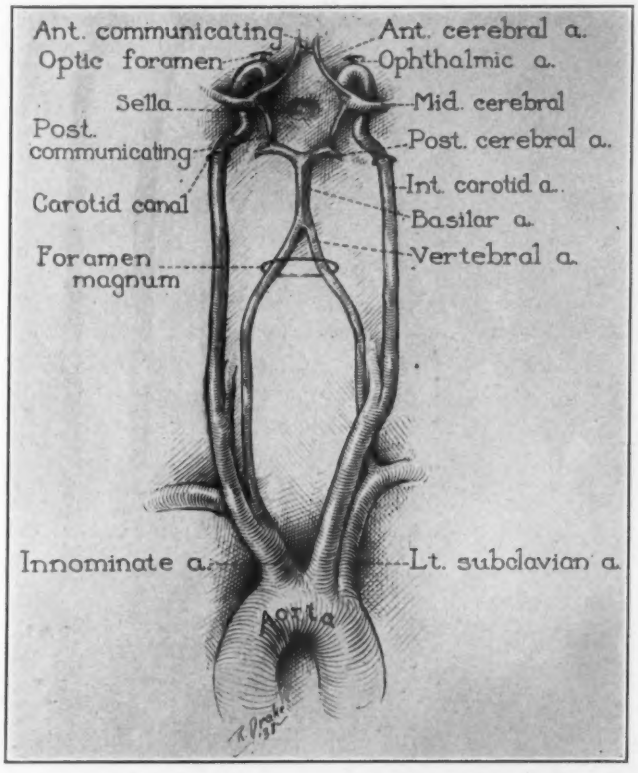

Fig. 6.—Sources of intracranial vascular supply with the relation of the vessels of the circle of Willis.

may press on the third nerve and cause ophthalmoplegia. Saccular aneurysms of the internal carotid artery within the sella are associated with a characteristic clinical picture, of which palsy of the third nerve, or ophthalmoplegia, is a most important localizing sign. Paralysis of the ocular muscles supplied by the fourth and sixth nerves also may occur, and pain in the region of the forehead and eye on the same side may be present because of the pressure on the ophthalmic division of the fifth, or trigeminal nerve. Pain in the cheek or jaw on the same side occurs occasionally because of pressure on the other divisions of the fifth nerve.

Intracranial aneurysms, besides producing pressure on contiguous brain and nerves, also may rupture, causing leakage of blood into the subarachnoid space, producing the well-known syndrome of spontaneous subarachnoid hemorrhage characterized by headache, vomiting, drowsiness and coma, associated with a bloody spinal fluid. Death frequently ensues. The diagnosis of intracranial aneurysm of the carotid artery is not difficult to make if the condition is kept in mind. Parker[4] pointed out that it is only in cases of aneurysm associated with intermittent leakage and focal compression that correct localization of the aneurysm is possible. A bruit, frequently associated with arteriovenous aneurysms, is rarely heard in cases of saccular aneurysm. The results of roentgenologic examination of the skull are often negative, but calcification of the wall of the aneurysm, unilateral erosion of the sella turcica, enlargement of the sella, unilateral enlargement of the optic foramen and the superior orbital fissure, erosion of the margin of the carotid canal, and displacement of the pineal body have been observed. Intracranial arteriography following injection of thorotrast into the carotid artery has proved of value in the diagnosis in some cases of intracranial carotid aneurysm. A negative result from arteriographic examination, as has been pointed out by Sjöqvist,[5] does not exclude the presence of an aneurysm, because thrombosis may occur in the aneurysm and fill the lumen.

In contrast with aneurysmal angioma, as regards etiology, it seems to be the consensus that most intracranial aneurysms are congenital, the aneurysmal path occurring on one or the other carotids or vessels comprising the circle of Willis. Tuffnell,[6] in 1853, drew attention to the probability that embolism was the starting point of cerebral aneurysm. Lebert,[7] in 1866, expressed the opinion that syphilis and the use of alcohol were not definite causes of this lesion, as had been supposed previously. Eppinger,[8] in 1887, first proposed that intracranial aneurysms arose as a result of a congenital defect in the muscular wall of the artery. Weber and Bode[9] suggested that the tendency of congenital defects to occur together was also a factor in the frequency of aneurysms in association with coarctation of the aorta.

The predilection of intracranial aneurysms for vessels in the base of the brain shortly after they enter the cranial cavity or at the point of bifurcation is constant. Most authors state that the middle cerebral artery is most frequently involved and that the basilar artery is next in order of frequency. In reviewing a total of 596 cases of aneurysm observed at the Mayo Clinic in the years 1925 to 1935 inclusive, Mills and Horton[10] found that 143 of the aneurysms were intracranial, 339 were intrathoracic, eighty were intra-abdominal, twenty-one involved the extremities, and thirteen were of a miscellaneous character. Syphilis was present in 3.5 per cent of the cases of intracranial aneurysm (which is

the normal incidence), in 70 per cent of the cases of thoracic aneurysm, in 8.8 per cent of the cases of intra-abdominal aneurysm, and in 9.5 per cent of the cases of aneurysm of the extremities.

Our usual impression of intracranial aneurysm is that the patient is perfectly well until the occurrence of headaches, sudden in onset and prostrating in character. These headaches probably are associated with a sinking spell from which he recovers, only to have a second and third attack. Illustrative of such a condition is the following case:

CASE 5.—A man, aged 52 years, came to the clinic complaining of headache, bitemporal in situation and severe in character. He had suffered from "stomach trouble" with epigastric pain, nausea, vomiting, and headaches for the previous three years. During these attacks he had sinking spells with exhaustion, followed by unconsciousness which continued for a period of several hours. In one of these attacks he was hurried to the hospital, where he complained of diplopia and headache; he vomited before he lapsed into unconsciousness.

Spinal puncture revealed the presence of bloody fluid; following spinal drainage he seemed to be slightly better. However, he had another attack the following day, and on the fourth day had a severe attack from which he did not recover. At necropsy an aneurysm of the right middle cerebral artery was found, together with evidence of multiple rupture and basal hemorrhages which accounted for his condition.

In selected cases, intracranial aneurysm is treated by ligation of the homolateral carotid artery in the neck. Ordinarily, ligation is considered only when the individual is less than 40 years of age. The patient must be able to withstand digital compression of the homolateral carotid artery for thirty minutes without the development of alarming symptoms and signs, thus demonstrating the presence of an adequate collateral circulation through the circle of Willis. Digital pressure can be applied by the patient, in the beginning, for five minutes three times a day, and gradually increased to two hours, three times a day. It must be emphasized that correct diagnosis, localization, and proper surgical treatment are fully as important in cases of intracranial aneurysm as in those of brain tumor.

Walsh and Love[11] recently have reported a case in which ligation of the carotid artery was performed. The patient was an automobile mechanic, aged 39 years, who, fifteen years previously, had noted attacks of mild headache and dizziness while at work. These attacks were intermittent, and four years after the initial attack, while at work, the patient suddenly became unconscious and remained so for several minutes. Ten years later while pumping up a tire he experienced a sudden, severe pain in the cervical region; this pain extended to the top of his head. His neck became rigid and moving his head caused severe pain. About forty-five minutes later he had a chill, his temperature was elevated, and he vomited. The headache persisted for about two weeks. This was fol-

lowed by blurring of vision and inconstant diplopia; the headaches became more severe. Constant ptosis of the right eyelid occurred.

The pupil of the right eye was dilated and fixed. The right eyeball had rotated downward and outward; it could not be elevated. Internal rotations were greatly limited, indicating the presence of a complete palsy of the third nerve. Otherwise, the examination gave negative results and no bruit was audible over the head. A diagnosis of intracranial, infraclinoid aneurysm of the right internal carotid artery was made.

It was found that digital pressure on the right carotid artery in the neck could be made for thirty minutes without producing abnormal symptoms and signs. Ligation of the right internal carotid artery in the neck was carried out, as well as ligation of the right internal and external jugular veins. After ligation of the carotid artery the patient stated that the headache, which had been one of his chief complaints, had ceased. The internal jugular vein was also ligated. Following operation, the patient was entirely relieved of his headaches and the function of the third nerve on the right side returned.

Because we are inclined to think of vascular intracranial lesions which simulate brain tumors as occurring in elderly people, the following case is reported. There are several factors about this case that are of interest. In the first place, the patient was a girl aged 20 years; in the second place, symptoms occurred following a serious automobile accident, and in the third place, the history simulated very closely that of onset of symptoms associated with tumor of the brain. To illustrate further how it simulated tumor of the brain, evidence of calcification was found on roentgenologic examination of the head; the shadow of calcification was irregular in outline, was not typical of a vascular lesion, and could have represented either tumor or an old hemorrhage. However, a loud, constant bruit could be heard over the entire right side of the head.

CASE 6.—A girl, aged 20 years, was brought to the clinic with the complaint of headache, mental sluggishness, and general malaise. Two years previously she had been in a serious automobile accident and had sustained a contusion on the right side of the head, but she did not lose consciousness. She returned to school the next day and remained well until six months later when, suddenly, she had a generalized convulsion, following which she had severe headache in the right temporal region. About ten days later she had another convulsion without aura. The headaches continued intermittently without convulsions until one year later, when she had another convulsion, following which she remained in bed for about a week, during which time she experienced a moderate degree of numbness and weakness of the entire left side of the body, including the face. Following this episode, the family noted a mental change. The patient appeared less alert than usual, was apprehensive, and sometimes slightly confused. She also observed a slight momentary taste aura, the character of which was not clear. Three months later, with the onset of one of the severe headaches, she vomited, was dizzy, and for the first time noted diplopia, which persisted. Following this, the headache was more persistent. She observed some hallucinations in the left field of vision, but was unable to describe them. About this time she became aware of a rushing sound in her head.

The patient was rather dull and cooperated poorly. The sense of smell was severely impaired on the right side. There was weakness of the sixth nerve on both sides. The movements of the body on the left side were somewhat slow and clumsy; the deep reflexes were hyperactive. The plantar responses were normal. On examination of the fundi, bilateral swelling of five diopters was found; the fields were normal. Roentgenologic examination of the head disclosed evidence of irregular areas of calcification in the right frontotemporal region. A loud, constant bruit, which could not be obliterated by pressure on either carotid artery, was heard over the entire right side of the head.

Through a right frontal exploration, large tortuous vessels were encountered extending down into the sylvian fissure. Following the operation there was increased weakness of the left arm and leg and left side of the face. This improved, and on the sixth day, while the patient was sitting up, a series of convulsions suddenly developed, following which she died.

The brain was found attached to the dura in the right middle cranial fossa, and the attachment proved to be the extremely dilated petrosquamous sinus (which normally is a very small sinus draining into the lateral sinus). It was greatly distended and emptied into the lateral sinus through an opening which was much narrower than the other portions of the cavity. The anterior end of the sinus emerged from a large, firm, rounded, nodular aneurysm which could be seen on separating the temporal and frontal lobes. The right middle cerebral artery extended laterally and curved around the posterior aspect of the aneurysm in the sylvian fissure. About 4 cm. from its origin it was in close contact with the mass, and when the artery was opened its lumen was found to communicate freely with the cavity of the aneurysm. The sylvian vein was also very much dilated and emerged from the upper surface of the same pouch of the aneurysm which was drained by the petrosquamous sinus.

It is difficult to make a preoperative diagnosis of an intrasellar aneurysm that produces the signs and symptoms of a basofrontal, intrasellar, or extrasellar tumor; only at operation can the diagnosis be made. Even then, the gross appearance is deceiving and it is necessary to insert a small needle into the mass.

CASE 7.—A man, aged 39 years, came to the clinic complaining of failure of vision. Two years previously double vision developed, and suddenly he lost the vision in the right eye. Vision returned in one month and seemed normal for six months. At that time he noted bilateral visual impairment which gradually increased during eighteen months until, five days before his examination at the clinic, his vision failed completely.

Neurological examination gave essentially negative results except for complete loss of vision in the right eye; perception of light was present in the temporal portion of the left field. The ocular reflexes were abolished and there was a bilateral choked disk with secondary optic atrophy; the choked disk measured three diopters in the right and four diopters in the left eye. Several small hemorrhages were seen in each retina. The defect in the field of vision suggested a previous right homonymous hemianopsia. Roentgenologic examination of the head revealed severe destruction of the sella turcica and posterior clinoids and, from study of the roentgenograms, a diagnosis of intrasellar tumor with suprasellar extension was made. A right transfrontal craniotomy was done. The brain pulsated normally and was under normal tension, which was out of proportion to the degree of papilledema present. The right frontal lobe was elevated easily and evidence of tumor in the

right basofrontal region could not be found. The optic chiasm was exposed easily and was presenting anteriorly, but remaining within the sella was a bluish pulsating mass which could be compressed when touched with forceps. This mass also could be seen lying lateral to the optic chiasm and extending posteriorly (Fig. 7).

A diagnosis of intrasellar aneurysm was made which explained the visual symptoms as well as the evidence of erosion observed in the roentgenogram of the head. The optic nerves were smaller than normal and examination revealed evidence of pressure atrophy. The patient did not receive benefit from the operation.

Intracranial aneurysms may simulate any other type of lesion clinically, and frequently it is difficult to distinguish them by roentgenologic studies. Intracerebral calcification may be associated with gliomas, hemorrhage, and dermoid cysts, as well as with an aneurysm. Sometimes it is necessary to explore the lesion to determine its pathologic nature.

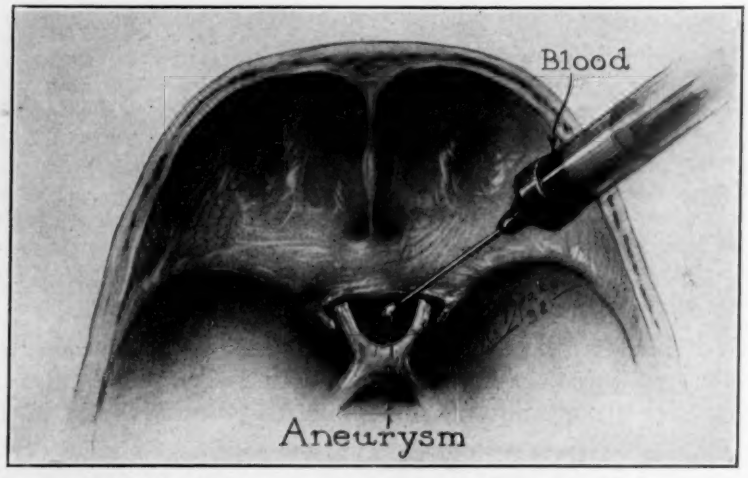

Fig. 7.—Intrasellar aneurysm simulating pituitary tumor.

CASE 8.—A man, aged 39 years, came to the clinic complaining of headaches and generalized convulsions which had occurred every four weeks for a period of thirteen or fourteen years, a constant pain behind the right orbit, blurring of vision, and weakness of the left side of the body. The headaches occurred almost every day, usually in the morning, beginning in the occipital region and extending over the entire head. The generalized convulsions usually began in the morning between 3 and 6 o'clock.

Neurological examination, including examination of the eyes, was entirely negative except for some slight weakness of both the left arm and left leg. Roentgenologic examination of the head revealed a large, calcified, cystic tumor above and behind the sella on the right side (Fig. 8). Because of the long history of slight weakness on the left side and the calcified lesion in the right middle fossa, it was thought wise to perform an exploratory operation. From the nature of the calcified shadow it was thought that either a calcified hematoma or a dermoid cyst would be found in the right temporal lobe. At operation, an incision was made in the superior temporal convolution, and at a depth of 2 cm. a large, calcified cyst wall was encountered. This was opened and was found to be filled with degenerat-

ing blood clot; this was removed completely. The thin, calcified wall could be resected easily from the surrounding brain by blunt dissection. The posterior half of the wall of the cyst was removed completely, but when the anterior wall was manipulated there was a sudden hemorrhage. This was controlled with packs, and the wound was closed. The patient died suddenly three days later. A large sacculated aneurysm of the right middle cerebral artery was found. Almost all of its calcified wall had been removed and the hemorrhage had occurred from a small opening between the artery and the calcified sac.

Intracranial aneurysms of the posterior fossa can simulate cerebellar tumors and lesions of the cerebellopontine angles, affecting the cranial nerves and compressing the contiguous pons and brain. Difficult to diagnose and distinguish from one another clinically, most of these lesions are identified at operation.

Fig. 8.—Calcified intracranial aneurysm of the right temporal lobe; *A*, anteroposterior view, and *B*, lateral view.

CASE 9.—A man, aged 37 years, came to the clinic complaining of weakness of the right side of the face and pain in the right eye. He was unaware of any weakness of the face until, eighteen months before he registered at the clinic, his children noticed that he slept with the right eye open. Shortly after this he was aware of the weakness of the right side of the face and it was diagnosed as Bell's palsy. One month before his examination he began to have occasional sharp pains in the right eye in addition to smarting or pain in the cornea. Examination, aside from the palsy of the seventh nerve and diminution of hearing on the right side, gave essentially negative results. Roentgenologic examination of the skull revealed an irregular erosion of the petrous portion of the right temporal bone mesial to the labyrinth and semicircular canal which appeared to be caused by a contiguous tumor. Because of the facial palsy and erosion of the contiguous bone, a unilateral suboccipital craniotomy was done and the right cerebellar lobe was elevated, allowing an excellent exposure of the cerebellopontine angle. Between the fifth and seventh nerves a large pulsating vessel, dark in color, could be seen compressing

both the seventh and eighth nerves and eroding the bone (Fig. 9). Evidence of tumor either of the cranial nerves or in this region could not be found. Following operation the patient did not improve clinically and was advised to have an anastomosis performed between the facial and spinal accessory nerves.

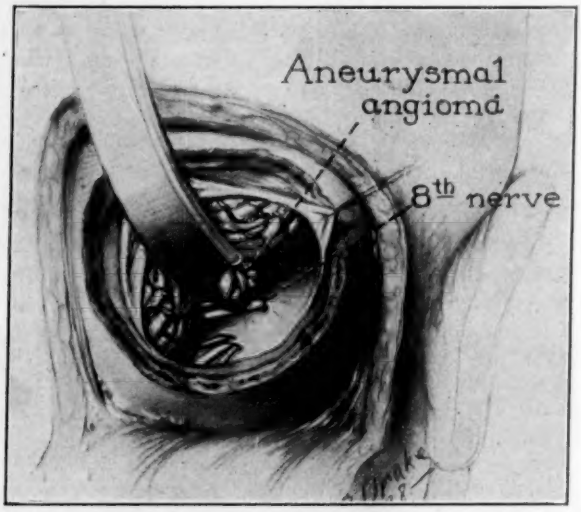

Fig. 9.—Aneurysmal angioma in the right cerebellopontine angle simulating tumor of acoustic nerve.

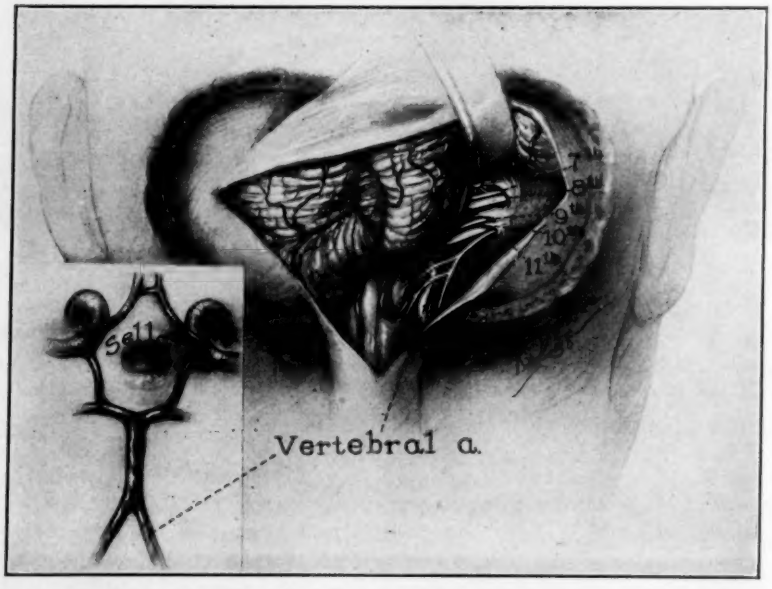

Fig. 10.—Aneurysm of the right vertebral artery simulating tumor of the right cerebellopontine angle.

A vascular lesion of the cerebellopontine angle, more extensive than that found in Case 9 and more closely simulating a tumor, was found in Case 10.

CASE 10.—A woman, aged 40 years, came to the clinic complaining of pain in the back of the neck, dizziness, staggering gait, and loss of hearing on the right side. Three and a half years previously, while suffering from a cold, she noticed that the hearing on the right was impaired. This had gradually become progressively worse. At about the same time, intermittent attacks of double vision began, associated with cramplike pains in the neck. Six months after the onset of the difficulty in hearing she began having a staggering gait. During the preceding year all the above symptoms were aggravated, particularly the staggering gait. The deafness progressed until the hearing was almost completely lost on the right side.

Examination of her eyes revealed slight diminution of vision in the right with normal vision in the left. Vertical nystagmus was noted. Papilledema and changes in the fields of vision were not found. Complete deafness of the right ear was present. The patient had such a severe degree of ataxia on the right that it was necessary for her to go about in a wheel chair. She held her neck stiffly and supported her head when sitting up or lying down. No bruit could be heard. The severe degree of ataxia on the right was associated with incoordination. A right suboccipital craniotomy was performed. Evidence of a tumor or an inflammatory lesion could not be found, but a large pulsating vessel could be seen compressing the pons, cerebellum, and cranial nerves. This vessel was an aneurysm of the right vertebral artery (Fig. 10). Associated with the aneurysm, the mesial surface of the cerebellum and pons was covered with a mass of telangiectatic vessels which involved the eighth, ninth, tenth, and eleventh nerves; this may have accounted for the patient's disability. Following her operation the patient had some temporary difficulty in swallowing and had to be fed through a tube. However, at the time of her dismissal her general condition was about the same as it was before operation.

COMMENT

Intracranial vascular lesions, although rare, so closely simulate tumor of the brain that a differential diagnosis is made with difficulty. Auscultation of the skull should be performed in every case of an intracranial lesion; if bruits are present, they usually signify the presence of a vascular lesion, although they may occur in association with tumors.

Aneurysmal angiomas must be treated conservatively, although it is sometimes necessary to ligate and cauterize the vessels. An intracranial aneurysm sometimes can be relieved, if the patient is young, by ligation of the carotid arteries, but digital compression should be performed first to determine whether or not untoward symptoms will develop from such a procedure.

Intracranial aneurysms can simulate cerebellar as well as cerebral tumors.

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THE EFFECT OF MEDIASTINAL LESIONS ON PRESSURES IN THE ANTECUBITAL AND FEMORAL VEINS

Report of Fifty-Two Cases*

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A NUMBER of investigators have called attention to the fact that comparisons of the blood pressures in the veins of the four extremities have considerable significance in the localization and diagnosis of diseases causing compression of the venae cavae or their branches. Among the most interesting of such conditions are those in which lesions of the mediastinum cause differences in venous pressures in the two arms or in the arms and legs. The close relationship of the superior vena cava to the ascending aorta and to the hilar region of the right lung explains the frequency with which aortic aneurysm and tumors of the right hilar region cause compression of the superior vena cava without affecting the inferior vena cava (Fig. 1). Similarly, the left innominate vein is easily encroached upon by aneurysm, and both innominate veins are susceptible of involvement in cases of tumors or other lesions in the superior mediastinum.

Middleton[1] reports a case of aneurysm of the aorta in which the venous pressure in the left hand was about twice as high as in the right hand, presumably because of obstruction to venous return. Villaret, Saint Girons, and Grellety Bosviel,[2] in their summary of the subject of localized venous hypertension, cite several cases in which the effect of mediastinal lesions upon venous pressure measurements is exemplified. In one case of aortic aneurysm the venous pressure in the left arm was 150 mm. of water higher than in the right arm, indicating compression of the left innominate vein. In 5 other cases of aneurysm the pressures were greatly elevated in both upper extremities, with normal readings in the internal saphenous vein in the 2 cases in which measurements were made at this point, indicating compression of the superior vena cava. Similar findings were recorded in two cases of mediastinal neoplasm, one a lymphoma and the other a metastatic carcinoma. Villaret and Martiny[3] review several cases in which the effect of aneurysm in altering peripheral venous pressures again is demonstrated. They also mention a case of tuberculous mediastinitis in which strangulation of the superior vena cava caused a pressure of 300 mm. of water in the veins of the arm as compared to a pressure of 200 mm. in the internal

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saphenous vein. Villaret and Desoille[4] mention difference in venous pressures in the arms as a common finding in cases of mediastinal tumors and cite a case of aortic aneurysm in which the venous pressures in the right and left arms, respectively, were 70 and 150 mm. of water. Ferris and Wilkins[5] report, among other interesting cases, three in which mediastinal tumors caused significant differences in the venous pressures of the arm as compared to those of the leg. One was a case in which the thyroid was substernal, with pressures of 105 and 50 mm. of water, respectively, in the antecubital and femoral veins. The second was a case of mediastinal chorionepithelioma invading the superior vena cava, with measurements of 230 mm. (antecubital) and 45 mm. (femoral).

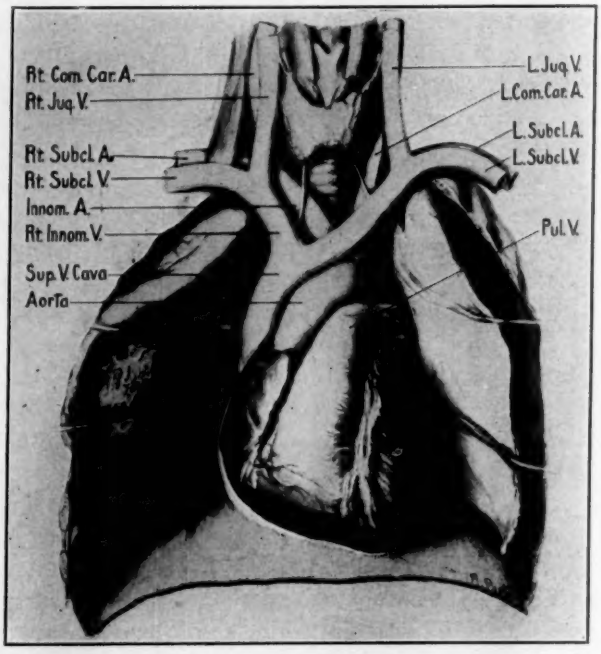

Fig. 1.—Anterior view of mediastinal structures.

The third was a case of bronchogenic carcinoma invading the superior vena cava, with measurements of 350 mm. (antecubital) and 80 mm. (femoral). Apparently, comparisons of the venous pressures in the two arms were not made in these cases. Burwell[6] reports a case of lymphoma of the superior mediastinum in which the venous pressures in mm. of water were as follows: Right antecubital, 360; left antecubital, 215; left femoral, 60.

In this present study, in which comparisons similar to those of the authors quoted above are included, venous pressure measurements were made by the method of Griffith, Chamberlain, and Kitchell.[7] A carpenter's level and a ruler were employed in order to ensure use of the same

plane on the two sides of the thorax and in the thigh for comparison of measurements. Readings were taken consecutively in the antecubital fossae and one of the femoral veins, the same instrument being used for each measurement on a given patient. The whole procedure required ten or fifteen minutes. This length of time is not sufficient to account for significant differences in pressures in the veins of the various extremities caused by alterations in the factors which normally control venous blood pressure, so that readings may be interpreted as if they had been taken simultaneously. Using this method in twelve patients without physical signs or roentgenographic evidence of disease which might cause alteration of the venous pressure in any of the extremities, I have found that the venous pressures in the two arms did not differ by more than 10 mm. of water in any case and that the pressure in the femoral vein tended to be a little higher than the pressure in the antecubital veins. In one case it was as much as 40 mm. of water higher, without apparent cause. These findings agree on the whole with those of Griffith, Chamberlain, and Kitchell[8] and of Burwell.[6] The series of fifty-two cases of mediastinal lesions in which clinical manifestations indicated the presence of a possible cause for differences in the venous pressures in the antecubital and femoral veins is included in Table I.

TABLE I

CASES IN WHICH THERE WAS A POSSIBLE CAUSE FOR DIFFERENCES IN VENOUS PRESSURE IN EXTREMITIES

	CASES
Aneurysm	27
Aortic dilatation	
Syphilitic aortitis	4
Hypertension	5
Mediastinal tumor (lymphoma)	7
Mediastinal tumor (carcinoma)	1
Undetermined	2
Superior sulcus tumor	1
Cold abscess	1
Substernal goiter	1
Carcinoma of esophagus	1
Patent ductus arteriosus	1
Pericarditis	1
	52

VENOUS PRESSURES IN CASES OF ANEURYSM

Venous pressure measurements were made in both upper extremities in 27 consecutive cases of aneurysm of the thoracic aorta or innominate artery, and in 18 of these cases measurement also was recorded in one of the femoral veins. Careful roentgenographic and fluoroscopic examinations were made in all cases as a part of the clinical study leading to diagnosis. The results of the venous pressure measurements are shown in Table II. In Cases 1 to 10, inclusive, the aneurysm involved the

ascending aorta; in Cases 11 to 17, inclusive, the aortic arch; in Cases 18 to 24, inclusive, both the ascending aorta and the arch; in Case 25, the descending thoracic aorta; and in Cases 26 and 27, the innominate artery.

In 23 cases (85 per cent) the venous pressure measurements in the upper extremities showed significant differences, ranging from 25 to 220 mm. of water. It is important to note that a significant difference in arterial blood pressures in the two arms is a much less common finding. A difference of 10 mm. of Hg, or more, in either systolic or diastolic pressure was found in only 7 of the 27 cases (26 per cent). This group includes the 9 cases in which measurements were not made in the femoral vein. In 5 of the 23 cases (21.7 per cent) the venous pressures were

TABLE II

VENOUS PRESSURES IN TWENTY-SEVEN CASES OF ANEURYSM

CASE NO.	VENOUS PRESSURES (MM. OF WATER)			CASE NO.	VENOUS PRESSURES (MM. OF WATER)		
	RT. ARM	LEFT ARM	FEMORAL		RT. ARM	LEFT ARM	FEMORAL
1	95	100	55	15	138	95	45
2	160	150	50	16	30	55	
3	250	210	45	17	170	200	
4	55	155	110	18	210	115	70
5	90	115		19	78	125	
6	238	275	45	20	165	160	85
7	15	85		21	205	210	60
8	80	50	45	22	120	205	50
9	300	120	60	23	220	150	
10	320	100	90	24	205	265	275
11	70	135	125	25	55	120	
12	60	270		26	150	65	60
13	85	160	100	27	90	25	45
14	84	122					

higher than normal in both arms, indicating severe compression of the superior vena cava or both innominate veins. In 10 cases (43.5 per cent) the venous pressure was higher than normal in one arm and normal in the other, indicating severe compression of one innominate vein without demonstrable compression of the superior vena cava and other innominate vein. In the remaining 8 cases (34.8 per cent) in which there were significant differences in pressures in the two arms, the pressures were all within normal limits, indicating probably slight compression of one innominate vein only. The venous pressure was higher on the left side in 14 cases (61 per cent), and higher on the right side in 9 cases (39 per cent). The preponderance of higher pressures on the left side probably depends on the anatomic fact already mentioned, namely, the closer relationship of the left innominate vein to the aorta. As would be expected, in both of the cases of aneurysm of the innominate artery the venous pressure measurements indicated compression of the right innominate vein only.

Of the 18 cases in which the pressure in the femoral vein was measured, the femoral venous pressure was significantly lower than the pressure in either arm in 10 cases (55.6 per cent), and in 8 cases (44.4 per cent) it was not. Included in the first group were the 4 cases in which a significant difference in the venous pressures in the two arms was not discovered. In only one case (Case 24) was the femoral venous pressure higher than normal. This patient had severe congestive heart failure which persisted until he died and precluded the possibility of a low femoral venous pressure. However, the arm pressures showed a significant difference of 60 mm. of water in spite of the congestive heart failure.

The conclusion to be drawn from these findings is inescapable. Aneurysm of the aorta or innominate artery practically always causes changes in the venous pressures in the extremities by compressing the

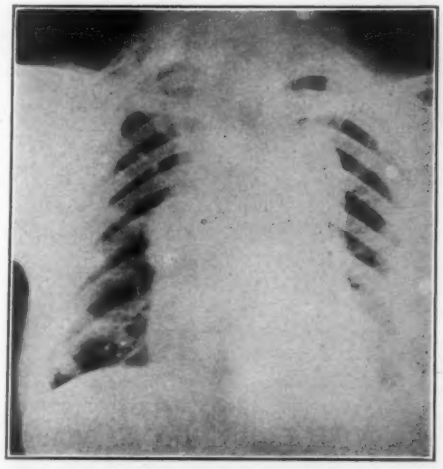

Fig. 2.—Case 22. Aneurysm of ascending aorta and arch.

superior vena cava or one or both of its main tributaries. The only important exception would arise in cases in which the aneurysm compresses only the superior vena cava and in which congestive heart failure is simultaneously present. In such cases the venous pressure would be high in the tributaries of the inferior vena cava because of the congestive heart failure, and there would be no significant difference in pressures in the tributaries of the superior vena cava on the two sides of the body. In general, the larger the aneurysm, the greater the differences in venous pressures in the extremities.

The diagnostic value of comparison of venous pressures in the extremities naturally will depend upon how often the procedure is used. Certainly it is simple and inexpensive enough to encourage its frequent use. Probably it should be used in all cases of aortic regurgitation in which roentgenographic examination is not contemplated. The following brief summary of a case of aneurysm demonstrates its value.

ILLUSTRATIVE CASE

CASE 22.—W. G., a negro, aged 60 years, was admitted to Gallinger Municipal Hospital March 17, 1937. He had been working as a furniture mover until one week before admission, when he had suffered a sudden attack of unconsciousness which came on while he was working. On recovering consciousness, after about 10 minutes, he had noticed that his right arm and leg were paralyzed. The remainder of the history was irrelevant except that he had had a chancre and inadequate antisyphilitic treatment many years in the past. Physical examination revealed the usual evidences of partial right hemiplegia. The arterial blood pressure was 200/100; there was hypertensive retinopathy, grade 2; the heart was slightly enlarged; and a murmur typical of aortic regurgitation was audible. There was slight edema of the left hand, believed at first to be the result of the hemiplegia.* However, the venous pressures in mm. of water were found to be 205 in the left arm, 120 in the right arm, and 50 in the femoral. These findings suggested the possibility of aneurysm or, as seemed less likely, some other mediastinal lesion causing compression of the superior vena cava and left innominate vein. Subsequent fluoroscopic and roentgenographic examination substantiated the diagnosis of aneurysm (Fig. 2).

VENOUS PRESSURES IN CASES OF AORTIC DILATATION

In 9 cases studied, aortic dilatation insufficient to constitute aneurysm was diagnosed on roentgenographic examination. The results of venous pressure measurements in these cases are shown in Table III. Syphilitic

TABLE III

VENOUS PRESSURES IN NINE CASES OF AORTIC DILATATION

CASE NO.	VENOUS PRESSURES (MM. OF WATER)		
	RIGHT ARM	LEFT ARM	FEMORAL
28	65	95	
29	130	130	90
30	160	125	60
31	80	105	
32	210	250	260
33	88	90	
34	170	175	170
35	50	55	
36	115	115	

aortitis was present in 4 cases, and severe hypertension in the other 5 cases. These causative factors accounted for 2 and 3 cases, respectively, in which significant differences were found in the venous pressure measurements. In the remaining 4 cases significant differences were lacking. Congestive heart failure was present in Cases 32 and 34 to account for elevation of femoral venous pressure. In the latter case repeated measurements of the venous pressures in the arms failed to reveal a significant difference, and the pressures dropped within normal limits as the heart failure improved. Apparently aortic dilatation alters peripheral venous blood pressure less commonly than aortic aneurysm.

*Unilateral edema on the paralyzed side is common, particularly in the upper extremity, in cases of hemiplegia. However, Weiss and Ellis[9] have shown that when such edema is the result of the hemiplegia the arterial and venous blood pressures are not significantly different in the upper extremities.

However, it must be kept in mind as a possible cause in cases in which comparisons of venous pressure measurements in the extremities are made for diagnostic purposes.

VENOUS PRESSURES IN CASES OF OTHER MEDIASTINAL LESIONS

In 16 cases of miscellaneous mediastinal lesions other than aneurysm or aortic dilatation, measurements of venous pressures in the two arms were compared, and in 13 of these cases measurement of femoral venous pressure also was obtained. The results of these measurements are shown in Table IV.

In 7 cases the diagnosis was mediastinal lymphoma, including 3 cases of Hodgkin's disease, 2 cases of acute lymphatic leucemia, 1 case of lymphosarcoma, and 1 case of malignant lymphoma of undetermined type. In this last case roentgenokymographic examination was necessary to exclude the diagnosis of aneurysm. In all 7 cases of lymphoma

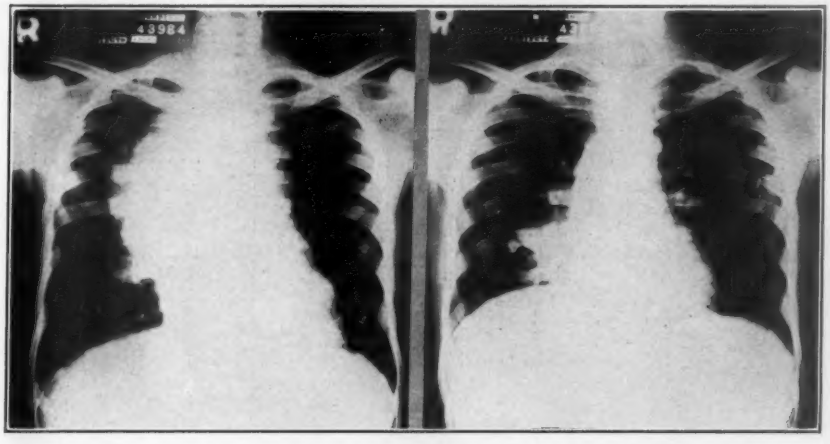

Fig. 3. Fig. 4.

Fig. 3.—Case 38. Hodgkin's disease before roentgenotherapy.
Fig. 4.—Case 38. Hodgkin's disease after roentgenotherapy.

the effects of compression of the superior vena cava or one of its main tributaries on the venous pressures in the extremities were evident. In 5 cases the venous pressure was considerably elevated and nearly identical in both arms and was within normal limits in the femoral vein, probably indicating compression of the superior vena cava. In the other 2 cases the venous pressure was higher than normal in one arm and within normal limits in the other arm and femoral vein, indicating compression of one innominate vein.

Several of the cases of lymphoma demonstrated a further use, mentioned in a previous report,[10] of comparison of repeated measurements of venous pressures for the purpose of showing the degree of response of mediastinal tumors to roentgenotherapy. For example, in one case of Hodgkin's disease (Case 38) with roentgenographic evidence of marked

enlargement of the mediastinum (Fig. 3), the venous pressures were 210 mm. in the arms and 100 mm. in the thigh. Several months later, after roentgenotherapy, the venous pressure measurements were as follows: right arm, 117 mm.; left arm, 93 mm.; femoral, 183 mm. This indirect evidence of shrinkage of the mediastinal tumor was verified by roentgenographic examination (Fig. 4). The rise in pressure in the femoral vein probably was the result of compression of the inferior vena cava by enlarged intra-abdominal lymph nodes.

In Case 44 the diagnosis during life was mediastinal lymphoma, probably Hodgkin's disease. The venous pressure measurements were indicative of compression of the superior vena cava, but no anatomic reason could be found for the high pressure (195 mm. of water) in the femoral vein. However, at post-mortem examination the patient was found to have carcinoma of the kidney (hypernephroma) with massive

TABLE IV

VENOUS PRESSURES IN SIXTEEN CASES OF OTHER MEDIASTINAL LESIONS

CASE NO.	DIAGNOSIS	VENOUS PRESSURES (MM. OF WATER)		
		RIGHT ARM	LEFT ARM	FEMORAL
37	Mediastinal lymphoma	55	195	60
38	Mediastinal lymphoma	210	210	100
39	Mediastinal lymphoma	175	80	45
40	Mediastinal lymphoma	160	160	80
41	Mediastinal lymphoma	190	190	45
42	Mediastinal lymphoma	235	235	50
43	Mediastinal lymphoma	180	180	55
44	Metastatic carcinoma	375	370	195
45	Undetermined	430	430	70
46	Undetermined	460	450	140
47	Rt. sup. sulcus tumor	180	50	60
48	Cold abscess	90	90	120
49	Substernal goiter	135	130	140
50	Cancer of esophagus	102	92	
51	Patent ductus arteriosus	90	120	
52	Pericarditis	320	130	

involvement of the mediastinal lymph nodes, accounting for the roentgenographic appearance of lymphoma, and with direct invasion and partial occlusion of the inferior vena cava, explaining the elevated pressure in the femoral vein.

Cases 45 and 46 were similar, as far as venous pressure measurements are concerned, to most of the preceding cases of mediastinal tumor; there was evidence of marked compression of the superior vena cava in the elevated, nearly identical venous pressures in the upper extremities, and normal pressure in the femoral vein. However, roentgenographic and fluoroscopic examinations yielded inconclusive results. In Case 45 the roentgenogram (Fig. 5) showed a shadow in the right superior mediastinum suggestive of a dilated superior vena cava, but the cause for this was not discovered. In Case 46 the clinical picture was that of sudden obstruction of the superior vena cava, with venous en-

gorgement and edema of the head, neck, and upper extremities. Roentgenographic and fluoroscopic findings were suggestive of an inflammatory lesion of the superior mediastinum, and this diagnosis was sup-

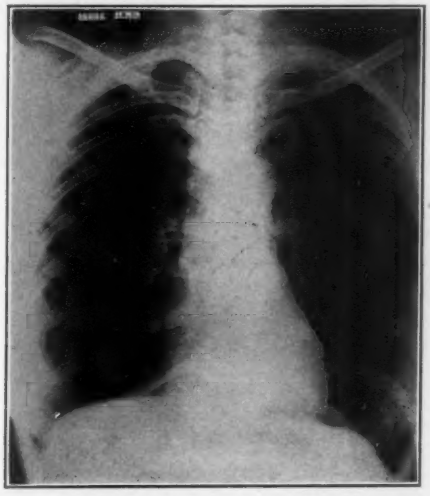

Fig. 5.—Case 45. Roentgenogram showing dilated superior vena cava.

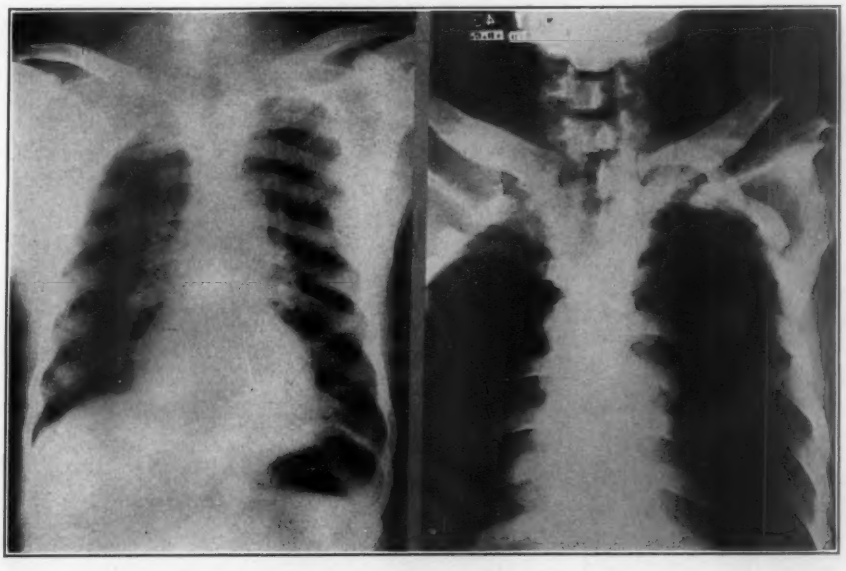

Fig. 6. Fig. 7.

Fig. 6.—Case 47. Right superior sulcus tumor.

Fig. 7.—Case 47. Roentgenogram showing destruction of right half of upper three dorsal vertebrae and first three ribs.

ported by the rapidity with which the patient grew worse and by the fact that death soon occurred. However, complete proof was lacking, and a post-mortem examination was not performed.

In Case 47, the patient, a 45-year-old negro, had symptoms and signs of disease of the upper thoracic portion of the spinal cord on the right side. He also had the ocular signs of involvement of the cervical sympathetic nerves on the right side. Roentgenograms disclosed an opacity overlying the apex of the right lung (Fig. 6) and destruction of the right half of the upper three dorsal vertebrae and posterior portions of the first three ribs (Fig. 7). The high venous pressure in the right arm probably indicated compression or invasion of the right subclavian vein. Biopsy of a cervical lymph node showed a highly undifferentiated malignant neoplasm. This finding, together with the roentgenographic report and failure to discover evidence of a primary neoplasm in the gastrointestinal tract, kidneys, or elsewhere, led to a diagnosis of superior sulcus tumor.

Little comment is necessary in Case 48, one of tuberculous abscess of the posterior mediastinum. The normal venous pressure measurements are not surprising in view of the distance of such an abscess from the great veins of the thorax.

In Case 49 comparison of venous pressure measurements in the upper and lower extremities had unusual diagnostic value. The patient, a white woman, aged 57 years, had the clinical manifestations of severe hyperthyroidism complicated by moderately severe essential hypertension. In the course of routine studies of the circulation the pressure in the antecubital veins was found to be above normal (150 mm. of water), and the arm-to-lung and arm-to-throat circulation times were prolonged (19 seconds and 36 seconds, respectively). These findings were believed at first to indicate the existence of congestive heart failure, but when roentgenographic study of the thorax showed a substernal goiter, the possibility had to be considered that elevation of venous pressure and prolongation of circulation times were due to compression of the thoracic veins. However, subsequent measurements of venous pressures in the femoral and antecubital veins all were high, confirming the original impression of congestive heart failure. In this case the femoral venous pressure was needed for accurate diagnosis.

In Case 50 the venous pressure measurements in the upper extremities were not significantly different. The patient, an Italian, aged 64 years, was obviously hoarse, but his other complaints could not be well understood partly because of the extreme hoarseness and partly because of his difficulty with the English language. The venous pressures were believed to rule out the possibility of aortic aneurysm in this case. The correct diagnosis of carcinoma of the esophagus was made after observing the patient for a few days and by means of appropriate fluoroscopic examination.

In Case 51, the patient, a young man, was known to have a patent ductus arteriosus. Venous pressure measurements were made in both arms as a matter of academic interest when it was discovered that no

arterial pulsations could be detected in the left upper extremity. Interestingly enough, the venous pressure was 30 mm. of water higher on this side than on the right. I have no explanation for these findings.

In Case 52 the patient, a white girl, had been ill for about a week with pneumococcal lobar pneumonia, when edema appeared in the right side of the face and right infraclavicular region. On the next day fluoroscopic examination of the thorax and pericardial paracentesis led to a diagnosis of suppurative pericarditis. Venous pressure measurements at this time in the right and left arms were 350 and 180 mm. of water, respectively. The following day a roentgenogram showed considerable compression of the right lung by the dilated pericardial sac (Fig. 8). On this day pericardiotomy was followed by a drop in the venous pressures to 320 mm. in the right arm and 130 mm. in the left.

Fig. 8.—Case 52. Massive pericardial effusion.

It seems likely that in this case the pericardial effusion, in addition to causing some compression of the superior vena cava or right atrium, distorted or compressed the right innominate vein. Post-mortem examination, almost two weeks later, disclosed no likelier explanation.

SUMMARY AND CONCLUSIONS

1. A review of the literature dealing with comparisons of venous pressures in the arms and legs in cases of mediastinal lesions is presented, and 52 original cases are reported.

2. In 27 consecutive cases of aneurysm of the aorta or innominate artery, there was a significant difference in the venous pressures in the two arms in 23 cases (85 per cent). In the remaining 4 cases, although the venous pressures were equal in the two arms, they were significantly higher than the pressure in the femoral vein. This finding of high

venous pressure in one or both arms and normal pressure in the femoral vein was present in more than half the cases (55.6 per cent) in which femoral venous pressure was measured.

3. Such alterations in venous pressure measurements are the result of compression of the superior vena cava or its tributaries without compression of the inferior vena cava. In general, the degree and type of alteration depend upon the size and location of the aneurysm.

4. Aortic dilatation insufficient to constitute aneurysm was observed in 9 cases, in 5 of which similar significant alterations in venous pressures were found.

5. The effects on venous pressures in 16 cases of other mediastinal lesions are presented. Such lesions, particularly tumors, are shown to alter venous pressure measurements in much the same way as aneurysm.

6. Repeated measurements of venous pressures are valuable in observing the response of some types of mediastinal tumor to roentgenotherapy.

7. Measurement of the venous pressures in the antecubital and femoral veins is a valuable aid in the diagnosis of mediastinal lesions.

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BILATERAL CAROTID SINUS DENERVATION IN A PATIENT HAVING SYNCOPAL ATTACKS AND A CONGENITAL VASCULAR ANOMALY

Report of an Unusual Case*

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THE following history of a patient suffering from syncopal attacks is presented because of the interesting combination of hyperirritability of the carotid sinus mechanism together with a congenital vascular abnormality affecting the head and upper extremities. The effects upon this syndrome of bilateral denervation of the carotid sinuses will be described.

REPORT OF CASE

I. S., a male Mexican laborer, 26 years of age, was admitted to the Santa Barbara General Hospital in July, 1935, with the complaints of fainting spells, visual disturbances, and transitory weakness of the arms and legs.

The family and past histories were irrelevant.

While picking lemons five months previously there was sudden loss of vision which lasted but a short time. This was followed by episodes of trembling of the hands, weakness of the legs, and foggy or double vision. These symptoms lasted only a few minutes, but occurred several times weekly and proved so incapacitating as ultimately to make work impossible.

On several occasions the visual disturbance was followed by momentary loss of consciousness which occurred most commonly when he was standing, occasionally after a heavy meal when sitting, but never when lying down. He did not believe that these atttacks were accompanied by convulsions, frothing at the mouth, or relaxation of the sphincters. Occasionally they were preceded by dyspnea. He had found that assuming a supine position prevented fainting and relieved the visual disturbance.

On physical examination neither blood pressure readings nor a radial pulse were obtainable in either arm. The blood and urine were normal. The spinal fluid was clear, not under increased pressure, and acellular. The colloidal gold curve was flat. Kahn precipitations, performed on blood and spinal fluid, were negative.

Six weeks later he was readmitted to the hospital because episodes of amblyopia, vertigo, and fainting, either singly or together, had recurred repeatedly.

The absence of pulsation in the major vessels of the upper extremities was again noted, and it was discovered that pressure over either or both carotid sinuses resulted in convulsive movements and syncope.

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The basal metabolic rate was minus 26 per cent. Venous blood sugar levels before and at hourly intervals following the ingestion of 100 gm. of glucose were 100, 117, 80, and 95 mg. per cent, respectively. Roentgenologic studies of the skull and chest disclosed a bony bridging of the sella turcica. There was no evidence of cervical ribs. The left ventricle was slightly enlarged, but the aortic arch was normal in pulsation and shape as viewed in the anteroposterior and oblique positions.

The patient was then referred to the vascular clinic of the Cottage Hospital where the following observations were made: There was pronounced pallor of the ocular fundi. A slight expansile pulsation, accompanied by a faint thrill, could be felt in the right carotid triangle. There was audible here a loud bruit with systolic accentuation which disappeared when pressure was applied just above the clavicle. The jugular veins were not visible. No pulsation could be felt over the left carotid artery, the temporal arteries, or the subclavian artery and its branches on either side. The blood pressure could not be obtained. Oscillometric readings on the arms were extremely low, the needle moving but half a division at the wrists. Vigorous pulsations were felt in the major arterial trunks of the legs and feet. The blood pressure in the legs averaged 220/120 when measured with the patient in the supine position.

To determine whether vascular spasm was an element in the production of this peculiar clinical picture, the patient, partially unclothed, was exposed to an environmental temperature of 18.2° C. for one hour, after which heat was applied to the trunk by means of a heated cradle. The temperature of the fingers of the right hand rose from 17.0° C. to 31.4°, and that of the fingers of the left hand rose from an initial level of 29° to 30.8° C. No increase in the oscillometric readings occurred after vasodilatation was induced, nor was it possible to obtain a pulse in the arms after giving nitroglycerin by mouth. It thus appeared certain that the lack of pulsation in the vessels of the upper extremities was not due to vascular spasm. The satisfactory rise in the skin temperature of the finger tips indicated that increase in blood flow to the hands, resulting from maximum vasodilatation, was of normal magnitude.

These observations suggested that the carotid and subclavian arteries took their origin from a common trunk arising from the aorta and that the orifice of this vessel was stenotic. Such an anomaly could explain the lack of pulsation in these vessels and the presence of the thrill and murmur above the clavicle.

Nature of the Syncopal Attacks.—Pressure over either carotid sinus resulted in seizures which the patient said were identical with his previous spontaneous attacks. The induced attacks were always similar in regard to the sequence of events and their time relationship with each other. Firm sustained pressure over either sinus area produced in four or five seconds slow, deep, regular breathing which persisted as long as pressure was maintained. Usually a few seconds later there was slight blanching of the face. The intensity, however, was difficult to evaluate because of the swarthy complexion. With continuance of pressure, tonic convulsive movements, appearing first in the legs, spread rapidly to the upper extremities, to be followed immediately by upward rotation of the eyeballs, dilation of the pupils, and, if the patient was sitting or standing, loss of consciousness. If pressure was still maintained, hyperpnea and convulsive movements persisted unabated. With release of pressure complete recovery was rapid, consciousness returning simultaneously with the subsidence of the other manifestations. The interval between the initiation of sinus pressure and the onset of syncope was usually about fifteen to twenty seconds. Light or intermittent pressure upon the sinus did not induce syncope nor convulsive movements, but some degree of hyperpnea always resulted. Likewise, syncope could not be induced if the patient was in the supine position.

TABLE I

CHANGES IN BLOOD PRESSURE AND PULSE RATE DURING INDUCED ATTACKS, SHOWING EFFECTS OF DRUGS AND OPERATIVE INTERVENTION

DATE	PROCEDURE	RESTING		PRESSURE RIGHT SINUS MAXIMUM CHANGE		PRESSURE LEFT SINUS MAXIMUM CHANGE		PRESSURE BOTH SINUSES MAXIMUM CHANGE		COMMENT
		BL. P.	PULSE RATE	BL. P.	PULSE RATE	BL. P.	PULSE RATE	BL. P.	PULSE RATE	
10/21/35		190/120	112	120-150/0	40-50	120/0	80-85	115/0	40	Hyperpnea, paling, tonic convulsive movements, syncope. Pressure either side gives similar sequence.
10/23/35	Epinephrine, 0.6 mg. intramuscularly	260+/140	104					135/0	60	Induced attacks not influenced by epinephrine.
10/29/35	Belladonna for 2 days. Atropine gr. 1/25 per os	205/120	84	185/100	100	170/100	84	175/95	64	Syncope could not be induced. Slight hyperpnea only with bilateral pressure.
10/31/35	Acetyl-β-methylcholine chloride 0.1 gm. intramuscularly	175/105	105					140/0	80	Hyperpnea and syncope easily induced.
11/26/35	Right denervation on 11/11/35	200/115	114	No change	No change	120/50	50			Pressure on right, no symptoms. Pressure on left, hyperpnea and syncope.
1/31/36	Left denervation on 1/8/36	180/90	105	No change	No change	No change	No change	200/105	84-80	Attacks can no longer be induced. Pulse slows slightly on bilateral pressure.

As previously stated, pressure over either sinus produced a similar train of events, but the concurrent changes in pulse and blood pressure differed slightly. With pressure upon the right sinus area, the systolic blood pressure as measured in the legs fell by as much as 40 to 80 mm. and the diastolic pressure usually became unobtainable. The pulse slowed to as few as 40 beats per minute. With release of pressure the rebound in blood pressure and pulse rate to the initial levels was immediate. Massage of the left sinus area was followed by a fall in pressure of similar magnitude, but the pulse slowing was less pronounced, averaging 20 beats per minute. With simultaneous pressure upon both sinuses there was some degree of summation of these effects. The magnitude of these changes is indicated in Table I. Electrocardiographic tracings taken during periods of maximum pulse slowing showed a simple depression of impulse formation in the sinus node. The rhythm remained regular and intraventricular conduction was unaffected.

The effect of various drugs upon induced attacks was studied. After the intramuscular injection of epinephrine, attacks could be induced with facility. The only change noted was that the pulse slowing was less pronounced. Atropin in large doses partially prevented the fall in blood pressure and pulse rate. Loss of consciousness could no longer be produced by bilateral pressure, and the hyperpnea was appreciably lessened. Acetyl-β-methylcholine chloride was used in large doses without appreciable influence upon the attacks. These observations are summarized in Table I.

Effect of Denervation of the Right Carotid Sinus.—On Nov. 11, 1935, denervation of the right carotid sinus was carried out under local anesthesia. The common carotid artery, just above the clavicle, was found to be slightly dilated and pulsating fairly vigorously. It then narrowed rather abruptly to approximately one-half the diameter of a normal artery, pulsation at this point and beyond being feeble. There was no communication between the artery and the jugular vein nor was the course of either vessel through the neck abnormal. Dissection of the carotid sheath and traction upon the artery in the region of the bifurcation caused hyperventilation and changes in the pulse and blood pressure which were exactly the same as those previously induced by pressure. Compression of the artery below the bifurcation was without effect. Electrocardiograms during these procedures were similar to those previously obtained. After the injection of novocaine about the sinus area periarterial stripping of the crotch was accomplished without further incident. Histologic examination of the removed tissue showed that it contained the carotid body and immediately related nerve fibers.

Course.—During the succeeding seven days in the hospital the blood pressure in the legs gradually rose from 185/95 to 225/135. On November 26, fifteen days after operation, the patient reported that he had been without symptoms except for one attack of vertigo and inability to flex the fingers of the left hand on the preceding day. At this visit the blood pressure, when the patient was supine, averaged 190/120. Firm pressure at the angle of the right jaw was entirely without result. During the succeeding month he had attempted to work, but his previous symptoms quickly returned with their former vigor. His pulse was found to be accelerated to 100 beats per minute, or more, on most occasions, as compared with the preoperative average of 80 to 90 beats per minute. The blood pressure in the legs remained at the same level. Pressure over the left carotid sinus area resulted in the usual attacks.

Denervation of the Left Carotid Sinus.—Because the patient's symptoms had not been appreciably improved by the first operation, the left carotid sinus was denervated on Jan. 8, 1936. Dissection of the neck disclosed a narrowed, pulseless, left common carotid artery. Its anatomic relationships with surrounding structures

were apparently normal. The dramatic course of events which occurred during the operation may best be expressed by the following protocol:

TIME	BLOOD PRESSURE	PULSE RATE	NOTES
9:10 A.M.	190/135		Excited; being prepared for operation.
9:30	260/140	129	Anesthesia of skin.
9:40	210/120	150	Dissecting sheath. Some hyperventilation.
9:50	160/110	135	Hyperventilation; sobbing and clenching of fists.
9:55	150/130	120	Artery being dissected out. Pulse suddenly slowed, then became imperceptible. Generalized tetanic convulsion. Pulse returned in about 30 seconds. Whiffs of carbogene.
10:02	190/150		Pulse slowing and weakening momentarily. Bifurcation dissected free.
10:03	190/150		Novocain into sinus.
10:13	260/150	150	Periarterial stripping begun.
10:35	260/160	132	Comfortable.
11:00	260/165	129	Dissection completed.

Course.—The patient has been observed over a fourteen-month period since the second operation. Blood pressure determinations were made at intervals of four hours during the first three postoperative days. The pressure remained at the preoperative level. During the succeeding month there were no syncopal attacks. For the following eight months the patient was able to work, but complained of transitory partial blindness and intervening periods when "things looked dark." At this time cataracts developed rapidly in both eyes, leading to total blindness. The cause of this unexpected complication remains unexplained.

Syncopal attacks, similar in all respects to those which occurred before operation have been experienced on approximately ten occasions. The last attack was followed by a left-sided hemiplegia from which recovery was complete in three weeks. At present pressure over either or both carotid bulbs is without effect upon respiration or blood pressure. The pulse slows slightly with bilateral pressure, but syncope can no longer be induced. The blood pressure in the legs as measured at frequent intervals during the fourteen-month period has shown a slight but definite downward trend. The last readings, taken with the patient in the supine position, averaged 160/100. The pulse rate has remained uninfluenced. It should be noted that this fall in pressure is not attributable to cardiac weakness.

DISCUSSION

It is not necessary to review the physiology of the carotid sinus mechanism except in so far as it bears upon derangement of the circulatory dynamics exhibited by this patient. Because of a vascular anomaly, the pressure within his sinuses was presumably low. If the sinus mechanism exerts a constant regulatory effect in the direction of preventing excessive intra-arterial pressures, the elevated blood pressure observed in the legs of this patient might be due to the lack of a pressure stimulus within the sinus sufficient to bring about a discharge of depressor impulses. Such a hypothesis at first sight seems reasonable in view of the fact that no rise in blood pressure occurred following denervation of

both sinuses. However, the studies of Leriche, et al.,[1] indicate that in man, as well as in the dog, the carotid sinus mechanism does not exert a constant regulatory effect upon the circulatory apparatus. They subjected five patients to bilateral carotid sinus denervation, and in three of these which were satisfactorily followed, changes in blood pressure and pulse rate were transitory only. Thus it would seem that the carotid sinus mechanism may be disrupted with impunity, so far, at least, as the danger of producing lasting hypertension or tachycardia is concerned. We may not, therefore, attribute the hypertension in our patient to inhibited sinus function. It is more likely that decreased flow through the vasomotor centers of the midbrain produced a state of generalized persistent vasoconstriction.

Two possibilities suggest themselves as explaining the occurrence of the syncopal attacks suffered by this patient. Cerebral ischemia, sufficient to induce unconsciousness, could conceivably result from sudden lessening of the carotid blood flow. This might occur when, in the upright position, the degree of physical activity did not insure the maintenance of a sufficiently high systolic pressure to drive the blood through the congenitally narrowed vascular system supplying the head. Such a mechanism would be similar to that in patients who faint from postural hypotension. The blood pressure in the legs of our patient rose 40 to 50 mm. when the upright position was assumed after lying supine, but, since pressures in the arm could not be obtained, we do not know whether a simultaneous diminution in blood flow occurred in the upper portion of the body, which, of course, is characteristic of postural hypotension.

The second possible mechanism is that at times a stimulus, the nature of which is unclear, acted upon the carotid sinuses and thus caused spontaneous attacks similar to those induced by pressure over the sinus areas. That such was the case seems probable. The patient stated that the subjective sensations accompanying the induced and spontaneous seizures were identical. Spontaneous attacks were preceded by difficulty in getting the breath, and on one occasion, after the patient had been standing for some minutes before a fluoroscopic screen, he began to breathe deeply and said that he felt dizzy and was about to faint. The hyperpnea continued for a minute or more, but consciousness was not lost. This was the only spontaneous attack seen by us. The appearance of the patient was similar to what it was during carotid sinus pressure. The complete disappearance of the spontaneous seizures for a month following the second operation and their infrequent occurrence since that time are likewise strong evidence that the carotid sinus was a factor. It is of course possible that both mechanisms were operative. This would explain the return of syncopal seizures, following operation, at a time when pressure upon the sinus areas was without effect upon the circulatory system.

Ferris, Capps, and Weiss[2] have classified carotid sinus syncope as being either of the cerebral type (syncope due to altered reaction of the brain cells dependent upon vasomotor changes in strictly localized areas or upon a response to efferent nervous impulses originating in the sinuses), or of the cardiac type (circulatory), in which unconsciousness is accompanied by, and presumably dependent upon, slowing of the heart and, usually, a fall in blood pressure. Fainting due to the latter mechanism is abolished by atropine. This was true in our patient, and the induced syncope was always accompanied by profound cardiovascular changes. He was therefore classified as an instance of the cardiac or circulatory type of syncope. Operative intervention was undertaken with the hope of interrupting this hypersensitive carotid reflex and of perhaps producing a lasting elevation of systolic pressure sufficient to drive blood through a congenitally narrowed vascular bed. The hope (although only partially realized) that by means of either or both of these effects a successful therapeutic outcome might be achieved justified surgical intervention of an experimental nature.

SUMMARY

Bilateral denervation of the carotid sinuses was performed upon a patient suffering from incapacitating syncopal seizures. The probable etiology of this condition was hyperirritability of the carotid sinus mechanism in association with a congenital obstruction to blood flow through the head and arms. The frequency and severity of attacks were greatly diminished over a period of fourteen months. Blood pressure and pulse rate levels were not appreciably altered. Bilateral cataracts developed after eight months, and a transient hemiplegia after ten months. Theoretic conceptions regarding the abnormal physiology in this case, and its attempted cure by surgical means, are discussed.

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THROMBOPHLEBITIS MIGRANS

Case Report

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THIS is a report of a case of thrombophlebitis migrans with unusual heart findings in which necropsy was performed. While these cases are not uncommon in the literature, post-mortem studies on them are rare.

CASE REPORT

Mrs. D. S., white, aged 54 years, was admitted to City Hospital on the service of Dr. W. L. Whittemore, in extreme heart failure, on May 25, 1937. Breathing was extremely difficult, cyanosis marked, the liver large and tender. Both legs were swollen and pitted on pressure. The right arm was swollen and warm. The blood pressure was not obtainable. The heart rate was 172 and the pulse rate 46, making a pulse deficit of 126. The following superficial veins were palpable as firm, pencil-like structures which could not be compressed: the right external jugular, right axillary, and all those of the right arm. The right axillary vein was tender to pressure. The legs were warm and had a red, blotchy appearance. Wherever veins were palpable, they were hard and incompressible. The diagnoses were (a) extreme heart failure and (b) multiple thrombophlebitis.

Eight cat units of digifolin were given intravenously. Within an hour the dyspnea was less pronounced, and the patient felt better. The heart rate was 140, the pulse rate 80, the pulse deficit 60. The pulse volume was good.

Additional History.—There had been moderate dyspnea and orthopnea for four years, becoming more severe during the preceding two weeks. The past history was otherwise negative except for diphtheria in childhood. The only treatment prior to the time of admission was "Christian Science."

Course.—Next day, May 26, the patient was given 8 cat units of digitan by mouth. The electrocardiogram (Fig. 1, *A*) was taken that evening. It showed ventricular tachycardia with a heart rate of 180. For the next three days the patient received 2 cat units of digitan and 0.2 gm. of quinidine daily, the latter to test for idiosyncrasy. The ventricular tachycardia and pulse deficit persisted (Fig. 1, *B, C,* and *D; D* was taken the morning of May 29). On May 29, 0.4 gm. of quinidine was given at 11:15 A.M., 1:15 P.M., 3:15 P.M., and 5:15 P.M., making a total of 1.6 gm. in six hours. Tracing *E* was taken in the evening; it showed numbers of nodal beats and a marked slowing of the heart. On May 30 the administration of quinidine in doses of 0.33 gm. three times a day was begun, with the result that normal sinus rhythm returned. Tracing *F*, taken May 31, and *G*, taken June 1, show this plainly.

With the appearance of sinus rhythm the pulse rate fell to 100, with no deficit, and the patient's condition was greatly improved. Quinidine in doses of 0.33 gm. three times a day maintained sinus rhythm. On two occasions when quinidine was discontinued ventricular tachycardia returned, and, with it, all the original symptoms. Each time quinidine in doses of 0.33 gm. three times daily restored sinus rhythm and brought about the same clinical improvement.

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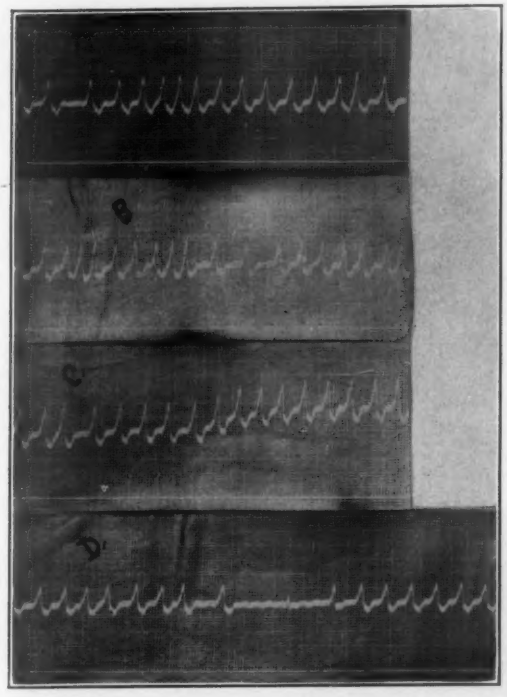

Fig. 1.—Lead I. *A*, May 26: after 8 cat units of digitalis, intravenously. Heart rate 180, radial pulse rate 40. *B*, May 27: digitalis, 8 cat units, total 16 cat units. Heart rate 180, pulse rate 80. *C*, May 28: digitalis, 2 cat units. *D*, May 29, morning: quinidine, 0.4 gm.

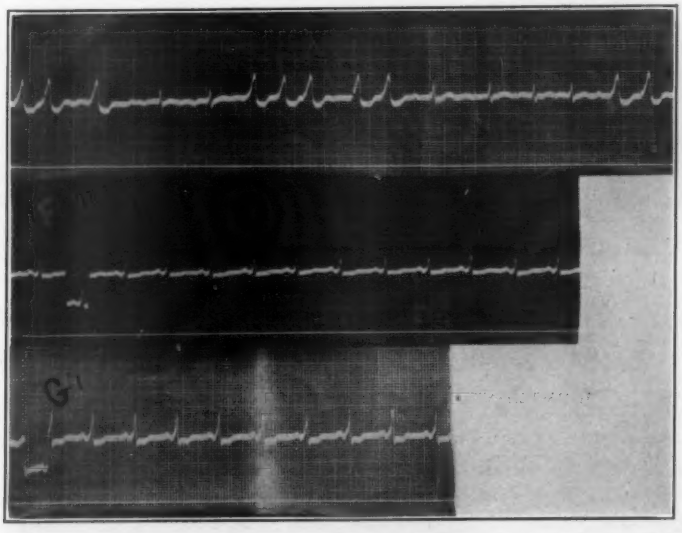

Fig. 1.—Lead I. *E*, May 29, evening: after 1.5 gm. of quinidine in divided doses. *F*, May 30: after additional quinidine (1 gm.). Heart rate 100, pulse rate 100. *G*, June 1: quinidine, 0.3 gm. three times a day. No pulse deficit.

During the remaining six weeks of her life the patient had a very difficult and eventful course. On four occasions she developed pain in the chest, fever, coughed up bloody, frothy sputum, and the lungs showed signs of consolidation.

The edema of the legs and right arm was at no time improved by diuretics, despite good diuresis. It subsided slowly and steadily, and the previously hardened veins softened.

On May 29 the left arm was painful, hot, and considerably swollen. These symptoms lasted for two weeks and then subsided slowly. On June 20, after a sharp temperature rise, two large abscesses of the back were drained.

The next episode was pneumonia with fluid in the chest. Dyspnea increased and the chest had to be tapped. The pleural fluid, at first serosanguineous, later became purulent and yielded indifferent streptococci on culture. Paracentesis was

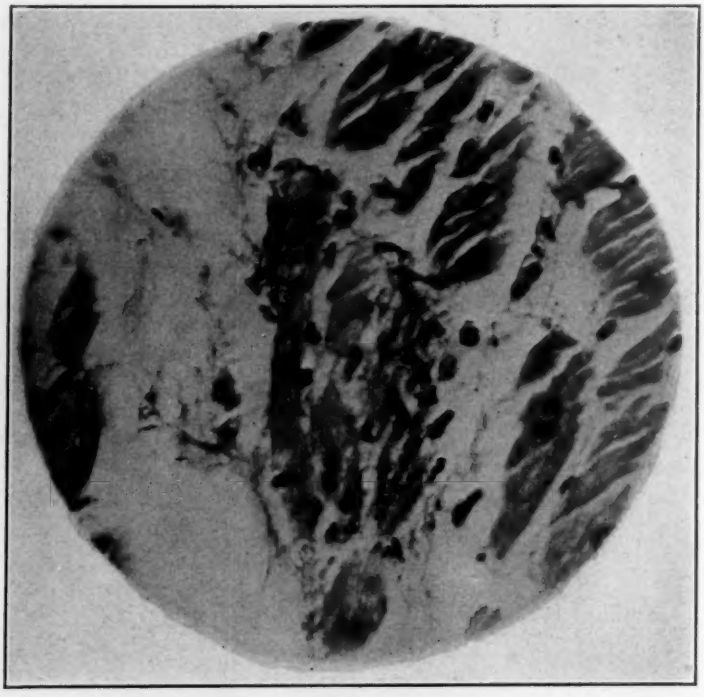

Fig. 2.—Minute area of myocardial degeneration showing early necrosis of the fibers and infiltration by polynuclear cells. View from left ventricle.

performed every three days. Soon the face and eyelids became swollen. At this time the plasma albumin was 1.7 per cent, the globulin 2.8 per cent, and the blood pressure 115/70. The urine contained leucocytes, erythrocytes, casts, and albumin (graded 2 plus).

On July 6 the temperature continued to rise. The patient was irrational, incontinent, and icteric (icteric index 25). The pulse and respiratory rates increased, and on July 11 she died.

Laboratory Studies.—The blood Wassermann and Kahn reactions were negative. On May 26 chemical examination of the blood showed nothing abnormal. On June 28 the blood chlorides were 379 mg. per cent. On June 4 the bleeding time was three and one-half minutes and the clotting time four minutes. On June 1 the hemoglobin was 60 per cent, the erythrocyte count 3,650,000, and the leucocyte

count 13,900. The differential leucocyte count showed 96 per cent polymorphonuclear neutrophiles (2 per cent of which were staff cells) and four per cent lymphocytes.

Autopsy (No. 4962).—There was moderate post-mortem rigidity. The finger nails were cyanotic. There was a greenish discharge from the nostrils. There were large decubital ulcers of the sacrum and right hip. The subcutaneous fat and muscles were normal. The peritoneum was dry and the abdominal organs were in normal position. The diaphragm was at the fourth right rib and fifth left interspace. Both external iliac veins contained ante-mortem gray-red adherent mural thrombi, extending down to the femoral rings and not completely occluding the lumina.

Heart: Weight, 375 gm. The sac contained 100 c.c. of clear fluid. The heart was moderately dilated, the epicardial fat normal in amount. The right chambers were normal, the valves not remarkable. The left auricle was enlarged, the endo-

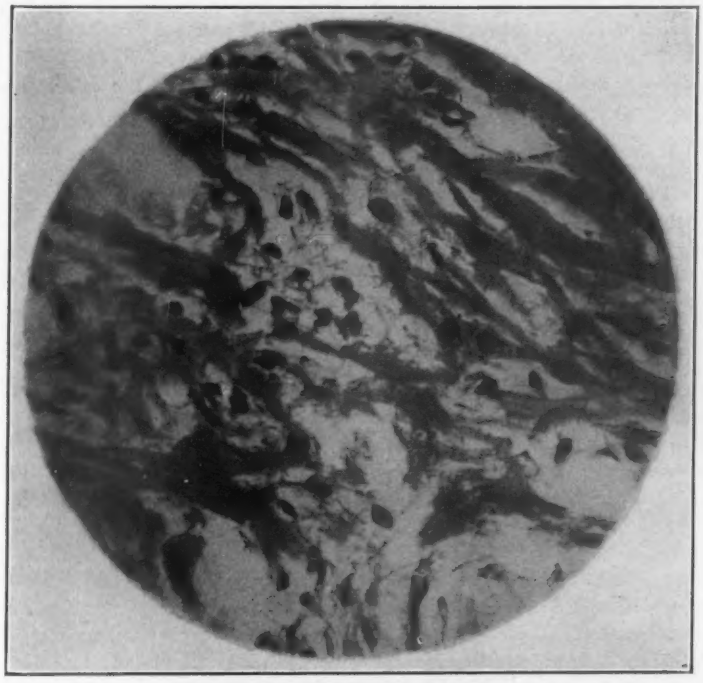

Fig. 3.—Lesion of similar nature in auriculoventricular node.

cardium thick, gray-white, and opaque. The mitral valve was stenotic, the cusps fused and leathery, the edges thick and rounded, the chordae tendineae short, thickened, and fused. Along the line of closure were several raised, soft, pinkish vegetations 2 to 3 mm. in size. The left and posterior aortic cusps were fused on the ventricular surface; the other cusps were normal. The myocardium was soft, flabby, pale yellow-red, of poor consistency and unscarred. The coronary mouths and arteries were normal.

Aorta: There was minimal atheroma, and the elasticity was well preserved.

Lungs: The right pleural cavity contained 200 c.c. of a cloudy fluid. The lobes were adherent by fine fibrous bands. The pleura was smooth and shiny. On section the color was pink. Scattered throughout all lobes there were small gray raised areas, and a moderate amount of exudate was present in the bronchi. The arteries and veins were free of thrombi. The weight was 800 gm.

The left pleural sac contained 1500 c.c. of greenish pus. The lung was collapsed against the vertebral column and covered by a thick green fibrinous exudate. On section the lower lobe was diffusely involved by a gray consolidation with small necrotic foci scattered throughout. No thrombi were demonstrable.

The bronchial lymph nodes were large, soft, and black.

Liver: Weight 1350 gm. It was moderately enlarged and soft. The gall bladder and ducts were normal.

Spleen: Weight, 100 gm. It was very soft. The cut surface presented a muddy gray appearance and the pulp scraped very easily.

Pancreas: Normal.

Adrenals: There was marked post-mortem disintegration.

Urinary System: The right kidney weighed 260 gm., the left 200 gm. In both kidneys there were several small cortical cysts and in the right there was a large subcapsular cyst measuring 5 cm. in diameter. The capsules stripped easily, leaving a smooth surface. The cortex appeared boiled, and the tissue markings were obscured. The pelvic mucosa was injected. The ureters and bladder were normal.

Internal generative organs: Except for a sessile polyp of the endometrium, the organs were not remarkable.

Gastrointestinal tract: Normal.

Histologic Examination.—Heart: The manifestations of rheumatic disease were in the final stage. There were numerous perivascular scars at the base of both ventricles and very few in the upper interventricular wall. In the left auricle there was a densely fibrosed subendocardial areolar zone. The mitral valve showed dense hyaline fibrosis, an occasional small calcified focus near the free edge, a few vascularized areas, and a vascular base wedge moderately infiltrated by small round cells. The left auricular muscle was greatly hypertrophied; the right ventricular, moderately.

The mitral valve showed a few fibrinous deposits on the auricular side.

Minute scars not associated with the vascular tree and apparently nonrheumatic in origin were found in the left ventricle. They were of all stages from well-vascularized connective tissue to dense hyaline scar.

Minute foci of acute myocardial changes were present in moderate numbers in both ventricles, the interventricular wall, and the auriculoventricular node. They involved small nests or individual fibers, which were replaced by a granular cytoplasmic mass invaded by polynuclear cells. In size and relationship to the vascular tree they resembled the small scars just described.

The arteries, veins, and endocardium presented nothing of note.

Lung: The lung was diffusely infiltrated by a fibrinopurulent exudate containing many gram-positive diplococci. There were very many areas of acute necrosis in the left lower lobe, without hemorrhage. Thrombi were not seen. Hemosiderin-bearing phagocytes were present in large numbers. Carbon pigment was dense in the perivascular and peribronchial regions, particularly at the hilum.

Liver: There were marked chronic passive engorgement and extensive fatty degeneration. The vessels were normal.

Kidney: Normal.

External Iliac Vein: Adherent to a portion of the wall was a young simple thrombus not undergoing organization. The wall, with the exception of destruction of the intima beneath the thrombus, was normal.

Anatomic Diagnosis.—Healed rheumatic myocarditis and valvulitis with mitral stenosis; acute myocardial focal degeneration; chronic passive congestion of lungs, liver, and spleen; acute bilateral pneumonia with empyema; anthracosis of lungs; acute cloudy swelling of liver and kidneys; decubital ulcers; multiple thrombophlebitis of superficial veins; bilateral thrombosis of external iliac veins.

REVIEW OF LITERATURE

Barker,[1] in a recent article, has given an excellent résumé of the literature on idiopathic thrombophlebitis which brings the subject up to the end of 1937. Up to and including 1935, twenty-two cases of this disease were recorded. For his study Barker selected seventy-nine out of 1,011 cases of thrombophlebitis. These seventy-nine were chosen because they occurred in patients in whom no demonstrable etiological factor such as infectious disease, a surgical operation, heart disease, varicose veins, or trauma was present. Half of the patients had a single attack, while the other half had recurrent attacks; one patient had had more than twenty episodes over a period of eighteen years. The veins involved included all the superficial veins of the body, arms, and legs. In 30 per cent of the recurrent cases there was pulmonary infarction, which was fatal in two cases. While no autopsy was obtained, Barker believed that the lung lesion was due to embolism from the veins of the extremities. Moorehead and Abrahamson,[2] in their series of four cases, reported lung involvement in two and thrombosis of the heart veins in one. Ryle[3] found in five cases one instance each of thrombosis of the lung veins and heart veins. Collier[4] and Ellison[5] record one case of pulmonary vein thrombosis. Campbell and Morgan[6] reported involvement of the cerebral and cardiac veins in a man 26 years of age. This patient's electrocardiogram showed rhythmic bigeminy. In Barber's[7] case the cerebral veins were the first to be involved. Walker,[8] Douglas-Wilson and Miller,[9] and Powell[10] reported a total of four cases, in all of which there was involvement of the superficial veins only. Harkavy's[11] patient had phlebitis of the veins of the left leg and thigh, and ascites. Six months later the left thigh was again involved. D'Abreu's[12] patient, a man of 52 years, had his initial thrombophlebitis in the left leg at 12 years of age. Then came later attacks at the ages of 43, 46, and 50. The terminal episode was gangrene of the right leg for which amputation was performed, following which the patient died. Autopsy revealed organized and canalized thrombi of the veins and arteries typical of thromboangiitis obliterans.

Idiopathic thrombophlebitis is a relatively benign condition, so that necropsy data on it are few. In the 101 cases cited above there was but one autopsy (D'Abreu's case). In eleven of Barker's cases, Barker removed a portion of thrombosed vein. Careful cultures of these remained uniformly sterile. Histologically, the lumen of the vein was occluded by an organized thrombus, and the wall of the vein was markedly infiltrated by connective tissue cells, as was the perivenous tissue. The process was indistinguishable from thromboangiitis obliterans except by the degree of reaction. These are the histologic changes of an end or late stage, which may account for the negative bacteriologic results. Barker stated his belief that the disease is strictly one of the peripheral veins and that visceral involvement is rare or nonexistent.

DISCUSSION

The patient of the present report was admitted to the hospital in extreme heart failure. She had thrombophlebitis of the following veins: right external jugular, right axillary, and all the superficial veins of the right arm and both legs. During her last seven weeks of life these cleared up slowly without residua. Four days after admission there developed a thrombophlebitis of all the superficial veins of the left arm which subsided after a course of two weeks.

The past history was one of moderate heart failure for four years, becoming severe during the two weeks before admission.

The course was interesting because of the four attacks of pulmonary infarction and the peculiar cardiac arrhythmia. These observations brought up the question whether or not we were dealing with visceral thrombophlebitis, especially of the pulmonary and cardiac veins. In the 102 cases of thrombophlebitis reported in the literature, pulmonary infarctions occurred in about 30 per cent. In the present case, definite clinical manifestations of infarction were present on four occasions, although none were demonstrated at necropsy. The presence of thrombosis of the iliac veins suggests that the emboli originated in the veins of the extremities. The absence of vascular disease in the lungs also supports the idea that the process was embolic rather than thrombophlebitic.

Thrombophlebitis of the coronary veins has been reported in a few instances.[2, 3, 6] In each of these cases, however, the diagnosis was entirely clinical and was based on electrocardiographic evidence of peculiar arrhythmias. In the one autopsy case, that of D'Abreu,[12] the coronary veins were not affected. In the present instance also, the heart was entirely unaffected by thrombophlebitis.

In the absence, then, of coronary thrombophlebitis, some other explanation must be sought for the persistent ventricular tachycardia. That the rheumatic disease was the etiological factor seems unlikely, since histologically there were only healed lesions with no evidence of activity, and the clinical course did not resemble that usually seen in congestive failure in a heart anatomically deformed by an old, inactive rheumatic process. There were present, however, widely distributed minute foci of myocardial necrosis in the ventricles and similar foci in the auriculoventricular node. It is recognized that damage to muscle, whether cardiac, voluntary, or involuntary, results in hyperirritability. Foci of potential irritability were found in this heart and, in addition, similar foci in the node governing ventricular contraction. The minute scars of different ages found in the ventricles corresponding in size and shape to the acute lesions suggests also that the process was a continuous one. Its duration would correspond to that of the persistent ventricular tachycardia, namely, the seven weeks the patient was under observation. The etiology of the lesion remains obscure. There is no evidence either to prove or disprove the presence of infectious or toxic factors.

The correlation between the clinical results obtained during the administration of digitalis and quinidine and the histologic changes in the myocardium yielded interesting and valuable information. This patient had a rare arrhythmia, ventricular tachycardia. In this state she was in extreme heart failure with a heart rate of 180 and an almost imperceptible radial pulse rate of 40. Full doses of digitalis improved the circulation, subjectively and objectively, without altering the rhythm, i.e., the dyspnea diminished and there was a marked improvement in the radial pulse; its rate rose to 80, it became stronger, and the pulse deficit decreased. Quinidine effected a prompt and dramatic improvement in this patient's circulation. One gram a day restored sinus rhythm at a rate of 100 and abolished the pulse deficit. On two occasions, when quinidine was discontinued, the original rhythm and circulatory failure returned. Each time quinidine again restored sinus rhythm and compensation. We were dealing, then, with a permanent ventricular tachycardia, controlled by quinidine, which makes this case rarer. It seems at first glance paradoxical that quinidine, a heart muscle depressant, could be used to increase the efficiency of the heart. It seems justifiable, however, to conclude that the depressant action served to inhibit overactivity from hyperirritable foci. The case shows clearly that we ought to use this remedy more often in properly selected cases.

SUMMARY AND CONCLUSIONS

1. A case of thrombophlebitis migrans with necropsy is presented.

2. The thrombophlebitis was found to involve only the veins of the neck, arms, and legs.

3. Phlebitis of the viscera was absent.

4. Pulmonary episodes in such cases are undoubtedly due to emboli, and not to phlebitis of the pulmonary veins.

5. A rare arrhythmia, permanent ventricular tachycardia, was not due to thrombophlebitis of the cardiac veins, but to another, coexisting lesion.

6. From the therapeutic standpoint, the heart muscle stimulating action of digitalis and the effectiveness of quinidine in depressing hyperirritable heart muscle were demonstrated.

7. Thrombophlebitis migrans is a relatively benign disease, without definite etiology and without visceral lesions.

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VENTRICULAR EXTRASYSTOLES INDUCED BY ELECTRICAL STIMULATION OF THE EXPOSED HUMAN HEART ROTATED THIRTY DEGREES COUNTERCLOCKWISE ON ITS VERTICAL AXIS

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THE recording[1] of ventricular extrasystoles induced by electrical stimulation of known sites in the exposed human heart has had a marked influence on our understanding of electrocardiography. Because of this newer conception of the electrocardiographic configuration of ventricular extrasystoles, the classical conception of the electrocardiographic configuration of bundle branch block was reversed.[2] The important basic work of Barker, Macleod, and Alexander[1] has been partly confirmed.[3, 4, 5] A report of experiments which confirm previous observations and add new information about this subject is herewith submitted.

REPORT OF CASE

The patient (D. M.), a white woman 39 years of age, had had advanced pulmonary tuberculosis involving the left lung since 1930. Pneumothorax was attempted on the left side in July, 1934, but was discontinued because of adhesions. A three-stage left-sided thoracoplasty was done in April and June, 1934.

Beginning in July, 1934, the patient complained of dyspnea upon exertion and of a pulling or pressure sensation around the heart. Cardiac physical examination after thoracoplasty was negative except for a systolic clicking sound heard at the apex of the heart and transmitted upward toward the base. This sound was heard only in the standing position and disappeared when the patient was lying down. It had not been heard previous to the thoracoplasty. The blood pressure was 110/76. The heart rate was 88 and the beat was regular. There were no other physical signs of cardiac embarrassment.

The cardiac diagnosis was pleuropericardial adhesions, and on July 29, 1937, an operation was performed by Dr. Richard Davison. At the time of operation the heart was freely exposed on its anterior and left lateral surfaces. The heart was found to be rotated counterclockwise on its longitudinal axis approximately 30°. This position gave free access to the left ventricle. There were some pleuropericardial adhesions which were severed. The pericardium was incised but no intrapericardial adhesions were found. During the operation the condition of the patient remained excellent. The exposed heart functioned in a normal manner. Recovery was uneventful.

Four accurately observed points on the surfaces of the ventricles were stimulated with single make and break shocks (make voltage 2.3 volts, break voltage 8 volts). The resulting ventricular extrasystoles were re-

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corded electrocardiographically in Leads I and III taken simultaneously with two electrocardiographs (Fig. 1). The four points of electrical stimulation were: Point one, located on the anterior wall of the base of the left ventricle; point two, on the anterior lateral wall of the left ventricle near the apex; point three, in the base of the posterior wall of the right ventricle 1.5 cm. to the right of the septum and posterior descending branch of the left coronary artery; and point four, on the anterior wall of the right ventricle about midway between Marvin and Oughterson's point *A* and Barker's point six.

Results of Stimulating Point One.—Point one was located on the anterior wall of the left ventricle near the base, about 1.5 cm. to the left of Barker's point one. Since the heart was rotated 30° in a counterclockwise direction on its vertical axis, this means that what would have been normally the posterior lateral basal region of the left ventricle was, under these circumstances, the anterior lateral basal region of the left ventricle. It may be observed that the configuration of the electrocardiogram from point one in this experiment has the same characteristics as that from Barker's[1] point one, which was taken with the heart in the normal position from the anterior lateral basal region of the left ventricle, whereas that from Lundy's point one (*1L*),[4] also taken from a heart in the normal position, has the opposite configuration in spite of the fact that the point coincides rather closely with point one stimulated in this experiment in which the heart is rotated 30° in a counterclockwise direction. This latter observation, when compared with the results of stimulating point one under the conditions of this experiment, gives clinical confirmation of the work of recent observers[5-9] who have shown that rotation of the heart within the thoracic cavity produces a change in the configuration of the electrocardiogram.

Results of Stimulating Point Two.—Point two was located on the anterior lateral wall of the left ventricle near the apex. Since the heart was rotated, this point corresponded to a point on the posterior lateral surface in a heart normally positioned. Point two was in the same region as Barker's point twelve, Marvin and Oughterson's[3] point *B*, and Lundy and Bacon's[4] point two. It is seen that with rotation of the heart 30° in a counterclockwise direction on the vertical axis, the electrocardiographic results are different. In our instance of point two the QRS complexes were divergent, with QRS in Lead I upright and QRS in Lead III inverted; while in the instance of point two of Marvin and Oughterson, they were convergent; QRS in Lead I was inverted and QRS in Lead III upright. The relationship of our results to those obtained by Barker from point twelve is mentioned under the discussion of our point two *A*.

It is important to observe that the results from stimulating points one and two support a previous experiment[10] in which the QRS deflections

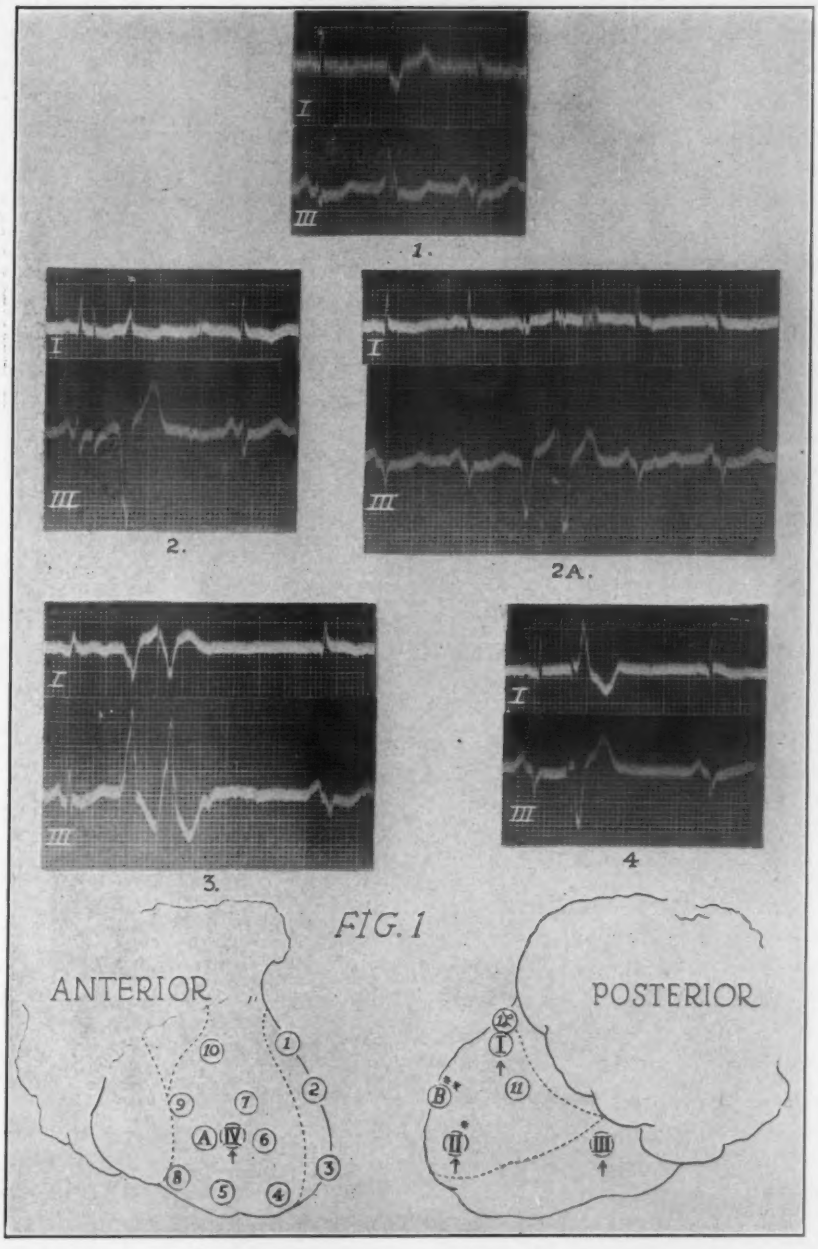

Fig. 1.—Points 1 to 12: Barker, Macleod, Alexander.
Points *A* and *B:* Marvin, Oughterson.
Points 1*L* and 2*L:* Lundy, Bacon.
Points I to IV: Arrows indicate points stimulated in these experiments.

***II and II*A* same as Barker's point 12.**
****2*L* same as point *B*.**

were opposite in direction in Leads I and III when derived from the base of the ventricles, in contradistinction to those derived from the apex.

Point two *A* was located in the same site as point two. This extrasystole was produced with the heart rotated approximately 30° in a clockwise direction on its horizontal axis when viewed from the patient's left side, in addition to the 30° counterclockwise rotation on its vertical axis, i.e., when the apex of the abnormally positioned heart rose up into the operative wound. It is to be observed that in this doubly rotated position the extrasystolic QRS complex is inverted both in Leads I and III like that obtained by Barker from his point twelve, which is in a similar location to our point two. The important difference in the conditions of Barker's and our experiment was that in Barker's case the heart was not rotated, whereas in our case and under the circumstances of this second stimulation of point two, the heart was not only rotated 30° counterclockwise on the vertical axis but was also rotated 30° in a clockwise direction upon the horizontal axis. This observation seems to show that the latter rotation caused QRS to become inverted in Lead I when the extrasystole arose at point two. Another important fact revealed by these sets of circumstances is that rotation about the horizontal axis influenced the extrasystole in Lead I and the *usual* electrocardiogram in Lead III. A suitable explanation for this fact might be that the pathway followed by the summation of electrical events which take place when an extrasystole arises at the apex of the left ventricle is in approximately the opposite direction to that taken when the excitation wave travels over the normal pathway.

Of course it must be admitted that there was considerable difficulty in keeping the electrode on exactly the same point with the heart beating, and still more so when the apex rotated temporarily into the operative wound. There was not so much difficulty encountered when the base was stimulated. However, it must be asserted that within reasonable limits our points were accurately located, since in both instances the same results were observed twice.

Results of Stimulating Point Three.—Point three was located on the base of the posterior wall of the right ventricle 1.5 cm. to the right of the septum and posterior descending branch of the left coronary artery. So far as we know this is the first time that this area has been stimulated in the exposed human heart. One may question these results because the first extrasystole was not produced by electrical stimulation, since there is no mark to indicate that such was the base, and because the second extrasystole would have happened regardless of the presence or absence of electrical stimulation. It is also true that pairs of spontaneously occurring extrasystoles arose even without mechanical stimulation in other instances during these experiments. However, it will be noted that the elapsed time between stimulation and ventricular response varied con-

siderably in our experiment; this is true in all cases reported in the literature, and, since it is possible for immediate response to take place, it is our feeling that this is a true ventricular extrasystole produced by electrical stimulation of the posterior basal region of the right ventricle. Furthermore, we should like to point out the similarity of mechanically and electrically induced ventricular extrasystoles when initiated from approximately the same areas. Two examples occur, in that Fossier's points five and six are practically identical with Barker's[1] points eight and two.

Results of Stimulating Point Four.—Point four was located on the anterior wall of the right ventricle near the apex, about midway between Marvin and Oughterson's point *A* and Barker's point six. Our result further confirms their observations. It is of great interest that in spite of the rotation of the heart, stimulation of this region of the right ventricle gave a ventricular extrasystole with the same configuration as those elicited from the same region of the right ventricle when the heart was in normal position. In this connection it is also important to recall that in Barker's work the configuration of extrasystoles from six different sites in a large area on the anterior surface of the right ventricle had similar configurations. In the left ventricle the configuration of extrasystoles from closely adjacent regions gave different configurations. With these facts in mind one would not expect rotation of the heart to influence the configuration of extrasystoles unless the amount of rotation were greater than the arc of a circle corresponding to the areas stimulated by Barker. Thus it would be expected that rotation of a few degrees would not influence the configuration of extrasystoles originating on the anterior surface of the right ventricle, whereas one would expect a change in configuration in extrasystoles arising from the left ventricle. The results of stimulation of points three and four on the right ventricle (in the presence of 30° rotation to the left on the horizontal axis), which were similar to those obtained by stimulating points one and two, show that the electrical axis of ventricular extrasystoles starting from the base of the right ventricle posteriorly is opposite to that of beats produced by electrical stimulation of a region near the apex of the anterior wall of the right ventricle.

DISCUSSION

It should be stated that a comparison of the electrocardiograms taken before operation and during the experiment failed to show any change in the QRS deflection in Lead I. In Lead III, in the instance of points one and two, QRS was more diphasic than in the control electrocardiogram, whereas the complex from point three was practically the same as the control before the stimulation, and inverted after the stimulation. Both before and after point four was stimulated, QRS in Lead III was inverted. This shifting of the QRS complex in Lead III was associated

with rotation of the cardiac apex up into the operative incision; the heart rotated about 30° on its horizontal axis at times during spells of rapid heart action (also during one short spell of paroxysmal ventricular tachycardia) and after the long pause following some extrasystoles, e.g., after stimulation of point three. In open-chest operations on dogs, as well as in humans, the heart likewise rotates about these two axes; this is independent of the individual heartbeat, but is probably related to the heart rate. We attribute the behavior to an increase in the amount of blood contained within the heart chambers at the end of the long pause following extrasystole, or to the accumulation of blood within the ventricular chambers due to inefficient emptying during tachycardia. We feel that in the case of point three this rotation of the heart on its horizontal axis occurred during the long pause following the extrasystole, and therefore did not complicate the electrocardiogram which was the result of stimulating that point, since the blood accumulation would take place after the extrasystole occurred. It might be repeated here that it is probably true that even if the heart had rotated up into the wound at the time the right ventricle was stimulated at point four, this amount of rotation would not have changed the configuration of the resultant electrocardiographic tracing. Upon study of the results of stimulation of these four points it is of interest to note that when only Leads I and III are observed, even though they are observed simultaneously, stimulation of point one gives a tracing which is indistinguishable from that obtained from point three, although the former originated in the left ventricle and the latter in the right ventricle; the only factor which they have in common is that they arose near the base of the ventricles, although this was from points at least six centimeters apart and separated by the septum. Similarly, point two cannot be distinguished electrocardiographically from point four, although they are located in the left and right ventricles, respectively. The only factor they have in common is that they were at about the same level near the apex of the heart. These observations tend to indicate that the site of origin of a ventricular extrasystole determines the configuration of the electrocardiogram according to its position in relation to the base or apex of the heart, not according to its location in one or the other ventricle. Likewise, in these observations it is shown that changing the point of stimulation from left to right on the ventricular surfaces does not determine the configuration of the electrocardiogram, since points one and two, respectively, are considerably to the left of points three and four, respectively, and yet the configurations are the same in the curves from points one and three as they are in those from points two and four.

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A STUDY OF THE TRANSVERSE DIAMETER OF THE HEART SILHOUETTE WITH PREDICTION TABLE BASED ON THE TELEOROENTGENOGRAM*

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SINCE Hodges and Eyster[1] described their formula for the estimation of the transverse cardiac diameter in man, many observers, notably Bainton[2] in America and Bedford and Treadgold[3] in England, have endorsed the transverse cardiac diameter as the most reliable index of heart size for all practical purposes. Many organizations, such as the New York Heart Association,[4] the American Heart Association,[5] and the Association of Life Insurance Medical Directors,[6] have similarly given their endorsements of this measurement of heart size. The original work of Hodges and Eyster was done on orthodiagrams, and many observers felt that with a simple correction the table could be adapted to teleoroentgenograms.

Dietlen,[7] Hammer,[8] and others have found an overestimation of 1 to 2.5 cm. in the transverse diameters of the heart on teleoroentgenograms when compared with those obtained by the orthodiagram.

Bedford and Treadgold suggest that teleoroentgenogram measurements should not be compared with orthodiagram measurements but that a different standard of normal size should be used for the method. Although they prefer the orthodiagram, claiming that the error in teleoroentgenography arises from difficulty in centering the patient accurately with reference to the film, in centering the tube accurately in relation to the heart, and in obtaining records always in the same phase of respiration, we have not encountered any such difficulty. On the contrary, we find it easier to train technicians to center the patient and tube and to take the films in midinspiration than to train physicians to make accurate orthodiagrams.

As a matter of fact, moving the tube either upward or downward or to the right or left a distance of 2½ inches makes very little difference in the final result with the teleoroentgenogram.

Our technique for making teleoroentgenograms is very simple. The standing position is used; the patient is placed directly in front of the plate holder, with his chin resting on its upper part. The dorsum of his hands are placed over his hips, which brings the scapulae away

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†Equitable Life Assurance Society.
‡Mutual Benefit Life Insurance Company.

from the thoracic cage and aligns his shoulders with the top of the plate holder. The tube is 6 feet from the subject, and the target is centered upon the spine at the level of the angle of the scapula. The exposure is made in one-thirtieth of a second, and the voltage is varied with the thickness of the chest. Care is always taken to see that the patient's face is turned neither to the left nor to the right, and emphasis is especially placed on having the ventral surface of the patient firmly opposed to the cassette or plate holder.

Since life insurance companies have adopted for general use the teleoroentgenogram in preference to the orthodiagram because the former also gives evidence of pulmonary disease if it is present, we have been experiencing increasing difficulty in applying the Hodges-Eyster formula. We have felt that our efforts to adapt this formula to teleoroentgenograms gave results which were not entirely consistent. Medical directors of other companies have had the same experience, and simultaneous applications for insurance to different companies have resulted in the issuance of policies with different premium ratings when identical films were furnished to all the companies concerned.

We have felt that the suggestion of Bedford and Treadgold was a good one—that new criteria, based on teleoroentgenograms, be established.

In a previous study,[9] one of us reported that the circumferences of the chest and abdomen vary with the index $\frac{\text{body weight}}{\text{height}}$, or $\frac{w}{h}$.

In another study,[10] it was suggested that a similar relationship might exist between the transverse diameter of the heart and the index $\frac{w}{h}$. Consequently, we felt that, since our applicants comprise a fairly representative sample of the population, including persons of all builds, ages, occupations, and social spheres, a study of their roentgenograms by means of this index would be desirable.

In the present study of the transverse diameter of the heart silhouette, we found that a similar relationship does actually exist between this diameter and the index $\frac{w}{h}$.

We have included in this study only the records of cases in which the systolic blood pressures fell between 110 and 145 mm. Hg and the diastolic pressures between 60 and 100 mm. Hg—a total of 1,460 cases. It is pertinent at this point to state that all the teleoroentgenograms used in this study were made under identical conditions in the Diagnostic Laboratory of the Equitable Life Assurance Society, according to the technique described above. We first determined for each subject, the height-weight index, $\frac{w \times 10}{h}$. The cards were then sorted

by indexes and for each index group the average transverse diameter of the heart was computed. The findings of this study are recorded in Table I. In column A the index $\frac{w \times 10}{h}$ is given; in column B, the number of cases falling within each index; and in column C, the average transverse diameter for each index.

TABLE I

A STUDY OF 1460 TELEOROENTGENOGRAMS

(INCLUDES ONLY CASES IN WHICH THE SYSTOLIC BLOOD PRESSURE RANGED BETWEEN 110 AND 145 MM. HG. AND THE DIASTOLIC BETWEEN 60 AND 100 MM. HG.)

A INDEX $\frac{W \times 10}{H}$	B CASES	C AVERAGE T.D. HEART (CM.)
15	1	10.4
16	4	10.8
17	12	11.0
18	32	11.7
19	61	11.8
20	88	12.3
21	118	12.3
22	179	12.8
23	188	13.1
24	198	13.3
25	142	13.7
26	159	14.0
27	97	14.0
28	75	14.2
29	38	14.5
30	28	14.7
31	24	15.1
32	6	14.9
33	7	15.0
34	1	13.8
35	2	14.4
	Total 1,460	(Average for all cases 13.277 cm.)

We have plotted Chart 1 with each index and corresponding average transverse diameter indicated by a cross. (The height-weight index average was carried to the first decimal point. This explains the position of the crosses in our graph, which, as will be noted, do not fall exactly on the index as given in Table I.)

The shape of the curve indicated by the points plotted in Chart 1 is a parabola with the axis vertical. It occurred to us, therefore, that possibly the function $\frac{w}{hd^2}$, in which "w" represents the body weight, "h" body height, and "d," the transverse diameter of the heart, might be constant, and a simple calculation indicated that, as a matter of fact, the value of this function is constant and is approximately 14.0 for all values of the index.

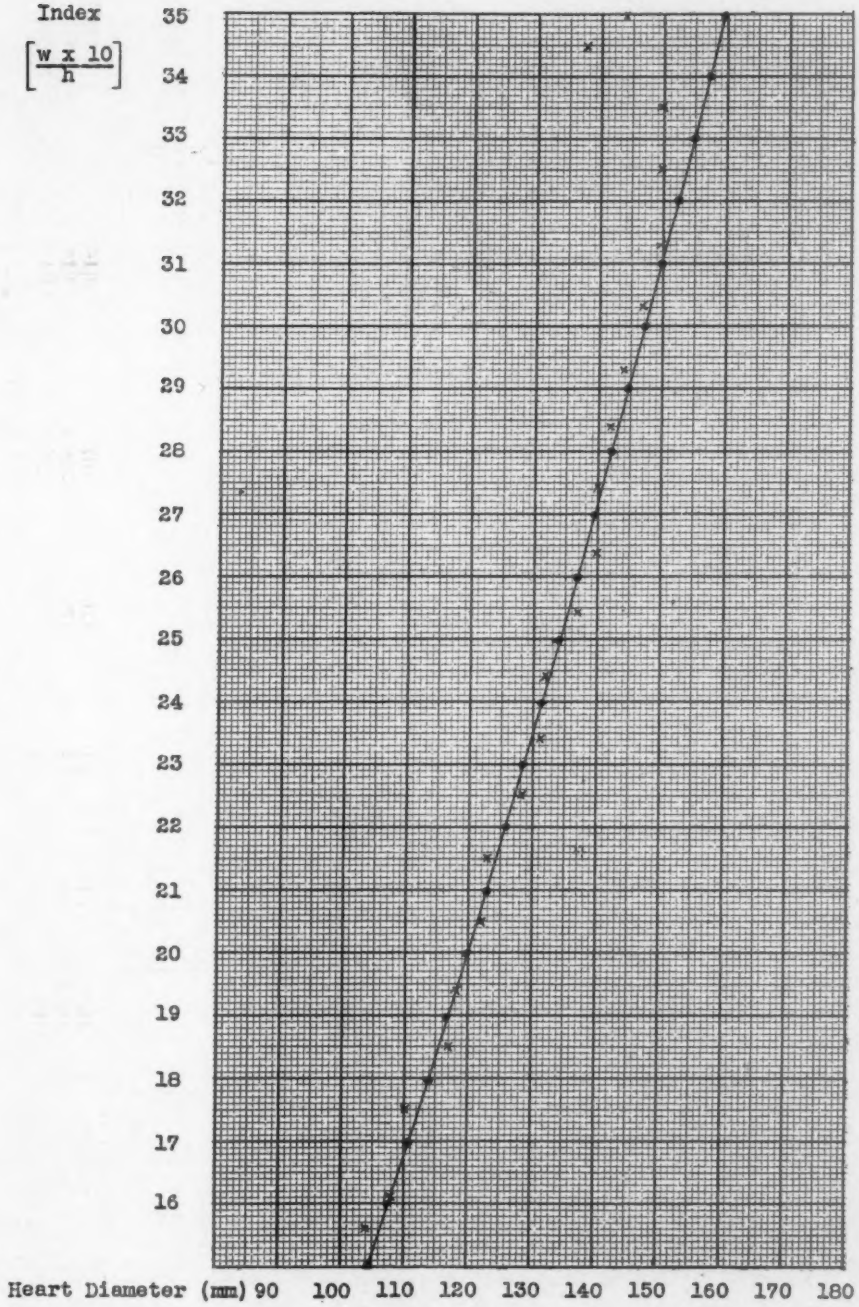
Index
$\left[\frac{w \times 10}{h}\right]$
35
34
33
32
31
30
29
28
27
26
25
24
23
22
21
20
19
18
17
16
Heart Diameter (mm) 90 100 110 120 130 140 150 160 170 180

Chart 1.

Table II

Theoretical Transverse Diameters of Heart Silhouette for Various Heights and Weights

T.D. of Heart	Height 5′0″	1″	2″	3″	4″	5″	6″	7″	8″	9″	10″	11″	6′0″	1″	2″	3″	4″	5″	6″
100 mm.	83	85	86	87	89	90	92												
101 "	85	86	88	89	91	92	93	95											
102 "	87	88	90	91	92	94	95	97											
103 "	88	90	92	93	94	96	97	99	100										
104 "	90	92	93	95	96	98	99	101	102										
105 "	92	93	95	96	98	99	101	103	104	106									
106 "	94	95	97	98	100	101	103	104	106	108									
107 "	95	97	99	100	102	103	105	106	108	110	111								
108 "	97	99	100	102	104	105	107	108	110	112	113								
109 "	99	101	102	104	106	107	109	110	112	114	115	117							
110 "	101	102	104	106	108	109	111	113	114	116	118	119	121						
111 "	103	104	106	108	109	111	113	115	116	118	120	121	123	125					
112 "	105	106	108	110	111	113	115	117	118	120	122	124	125	127	129				
113 "	106	108	110	112	113	115	117	119	121	123	124	126	128	129	131	133			
114 "	108	110	112	114	115	117	119	121	123	125	126	128	130	132	133	135	137		
115 "	110	112	114	116	117	119	121	123	125	127	129	130	132	134	136	138	140	141	
116 "	112	114	116	118	120	121	123	125	127	129	131	133	134	136	138	140	142	144	146
117 "	114	116	118	120	122	124	125	127	129	131	133	135	137	139	141	143	144	146	148
118 "	116	118	120	122	124	126	128	129	131	133	135	137	139	141	143	145	147	149	151
119 "	118	120	122	124	126	128	130	132	134	136	138	140	142	143	145	147	149	151	153
120 "	120	122	124	126	128	130	132	134	136	138	140	142	144	146	148	150	152	154	156
121 "	122	124	126	128	130	132	134	136	138	140	142	144	146	148	150	152	154	156	159
122 "	124	126	128	130	132	134	136	138	140	143	145	147	149	151	153	155	157	159	161
123 "	126	128	130	132	134	136	139	141	143	145	147	149	151	153	155	157	160	162	164
124 "	128	130	132	134	137	139	141	143	145	147	149	152	154	156	158	160	162	164	166
125 "	130	132	134	137	139	141	143	145	147	150	152	154	156	158	160	163	165	167	169
126 "	132	134	137	139	141	143	145	148	150	152	154	156	159	161	163	165	167	170	172
127 "	134	137	139	141	143	146	148	150	152	154	157	159	161	163	166	168	170	172	175
128 "	136	139	141	143	146	148	150	152	155	157	159	161	164	166	168	171	173	175	177
129 "	139	141	143	146	148	150	152	155	157	159	162	164	166	169	171	173	176	178	180

Refer to paper entitled "A Study of the Transverse Diameter of the Heart Silhouette with Prediction Table Based on the Teleoroentgenogram" presented to the Association of Life Insurance Medical Directors of America by Dr. Harry E. Ungerleider of the Equitable Life Assurance Society, and Dr. Charles P. Clark, of the Mutual Benefit Life Insurance Company. (1938.)

Table for Determining the Per Cent Deviation from Average

Minus 25 %	20 %	15 %	10 %	5 %	Av'ge %	Plus 5 %	10 %	15 %	20 %	25 %
75	80	85	90	95	100	105	110	115	120	125
76	81	86	91	96	101	106	111	116	121	126
77	82	87	92	97	102	107	112	117	122	128
77	82	88	93	98	103	108	113	118	124	129
78	83	88	94	99	104	109	114	120	125	130
79	84	89	95	100	105	110	116	121	126	131
80	85	90	95	101	106	111	117	122	127	133
80	86	91	96	102	107	112	118	123	128	134
81	86	92	97	103	108	113	119	124	130	135
82	87	93	98	104	109	114	120	125	131	136
83	88	94	99	105	110	116	121	127	132	138
83	89	94	100	105	111	117	122	128	133	139
84	90	95	101	106	112	118	123	129	134	140
85	90	96	102	107	113	119	124	130	136	141
86	91	97	103	108	114	120	125	131	137	143
86	92	98	104	109	115	121	127	132	138	144
87	93	99	104	110	116	122	128	133	139	145
88	94	99	105	111	117	123	129	135	140	146
89	94	100	106	112	118	124	130	136	142	148
89	95	101	107	113	119	125	131	137	143	149
90	96	102	108	114	120	126	132	138	144	150
91	97	103	109	115	121	127	133	139	145	151
92	98	104	110	116	122	128	134	140	146	153
92	98	105	111	117	123	129	135	141	148	154
93	99	105	112	118	124	130	136	143	149	155
94	100	106	113	119	125	131	138	144	150	156
95	101	107	113	120	126	132	139	145	151	158
95	102	108	114	121	127	133	140	146	152	159
96	102	109	115	122	128	134	141	147	154	160
97	103	110	116	123	129	135	142	148	155	161

| | | |

It appears, therefore, that a satisfactory evaluation of the crude data will be obtained by assuming the stated function to be constant. The actual value of the constant was determined in the following way:

Average weight = 165.83 pounds
Average height = 68.04 inches
Average diameter = 132.77 mm.

(In order to obtain a constant with two digits, we multiplied the weight by 100,000.)

Our constant is, therefore,

$$\frac{w \times 100{,}000}{h(d)^2} = \frac{165.83 \times 100{,}000}{68.04\ (132.77)2} = 13.83$$

If men of different weights and heights were built in proportion to perfect cylinders, tables for all body circumferences and diameters could be constructed by the use of constants, e.g.,

$$\text{For diameters,} \qquad C = \frac{w}{hd^2}$$

$$\text{or for circumferences,} \quad C = \frac{w}{hc^2}$$

In a previous study, one of us found that the chest circumferences almost follow such constants, but the abdominal circumferences do not because of the fact that these circumferences are much affected by the amount of adipose tissue present. Therefore, our table for chest and abdominal circumferences was constructed by using the index $\frac{w}{h}$ in the manner shown in our original paper.

We have found, however, that the heart diameter so closely follows a constant, as is shown later, that such a constant can be used in the development of a table for heart diameters. On the other hand, the internal chest diameters do not follow such a constant, but more nearly follow a constant $\frac{\sqrt{wh}}{hd^2}$. Therein lies the chief fallacy in attempting to correlate heart diameters with the internal diameters of the chest.

With this value for our constant, we next proceeded to compute for each index included in Chart 1 the theoretical transverse diameter. These values are indicated by dots and connected by a solid line. It is evident that the curve thus produced represents a satisfactory graduation of the original data, and the constant thus found was accordingly adopted as suitable for the development of a table of standard diameters for all heights and weights.

By the use of this constant we next developed Table II, which gives the theoretical transverse diameters in millimeters for heights 5 ft. 0 in., to 6 ft. 6 in., inclusive, and for the weights commonly found for each height. It should be noted that in the original group of subjects the heights were taken in shoes, and the weights included all clothing

except coat and vest. The directions for use of the table are simple. Find in the table the height column corresponding to the height of the individual under consideration. Below, in that column, find the nearest weight. To the left on that line will be found in the first column the theoretical transverse diameter of the heart silhouette.

Our first problem in testing this table was to determine how closely the theoretical diameters corresponded at all points with the actual diameters found in the original material. In general, it may be stated that short men—those under the height of 68 inches—were found on the average to have diameters 1 to 2 mm. greater, and tall men—those over the height of 68 inches—1 to 2 mm. less than the theoretical. At no point in the table, however, does it appear that the deviation of actual from theoretical will average more than 1 or 2 per cent. We concluded, therefore, that it was unnecessary to make any correction for height.

The next problem was to determine whether, in the use of the table, any correction need be made for age. In Table III are recorded the results of this study. In column A, we find the age groups; in column B, the number of cases falling into each group; in column C, the total deviations (plus or minus, recorded separately) of actual transverse diameters from the predicted given in Table II; in column D, the difference between plus and minus deviations in column C; and in column E, those differences divided by the number of cases in the respective groups shown in column B.

TABLE III

EFFECT OF AGE ON TRANSVERSE DIAMETER OF HEART

A	B	C		D	E
AGE (YR.)	CASES	DEVIATIONS (MM.)		DIFFERENCE BETWEEN + AND − IN COL. C (MM.)	CORRECTION FOR AGE (MM.)
		+	−		
15-29	123	514	501	+ 13	+0.1
30-39	293	1,185	1,294	−109	−0.4
40-49	571	2,544	2,261	+283	+0.5
50-59	358	2,118	1,441	+677	+1.9
60-70	115	661	510	+151	+1.3
Total	1,460				

It is obvious that no correction need be made for ages between 15 and 50 years. At later ages, the deviation from the theoretical is very slight, calling for only (approximately) a 1 per cent correction of the theoretical given in the table. Furthermore, such deviation as is shown in the above study (Table III) is probably the result of actual abnormality in a few cases included in the original material. It does not, therefore, appear necessary to make any correction for age.

Table IV gives the results of a study of the effect of blood pressure on the transverse diameter of the heart. This study was made on a

group of 2,192 subjects, all applicants for life insurance, but not necessarily accepted as insurance risks. In column A are noted the various blood pressure groups; in column B, the number of cases falling within each group; in column C, the total deviations (plus or minus, recorded separately) of actual transverse diameters from the predicted given in Table II; in column D, the difference between plus and minus deviations in column C; and in column E, those differences divided by the number of cases in the respective groups shown in column B.

TABLE IV

EFFECT OF BLOOD PRESSURE ON TRANSVERSE DIAMETER OF HEART (2,192 CASES)

A SYSTOLIC BLOOD PRESSURE (MM.)	B NUMBER OF CASES	C DEVIATIONS (MM.) +	C DEVIATIONS (MM.) −	D DIFFERENCE BETWEEN + AND − IN COL. C (MM.)	E DIFFERENCE IN COL. D DIVIDED BY CASES IN COL. B (MM.)
109 and under	82	396	366	+ 30	+0.4
110-119	300	1,403	1,241	+162	+0.5
120-129	456	1,826	2,061	−235	−0.5
130-139	437	2,255	1,829	+426	+1.0
140-149	390	2,230	1,353	+877	+2.2
150-159	267	1,462	890	+572	+2.1
160-169	174	1,146	508	+638	+3.7
170-200	86	642	167	+475	+5.5
Total	2,192				

When the systolic blood pressure is below 130 mm. Hg the transverse cardiac diameter is normal. Above that level there is a slight though definite indication of increasing hypertrophy with increasing hypertension. It is worth noting, however, that this increase in the transverse diameter would not be noted by percussion, an observation made many years ago by Janeway in the study of essential hypertension.

As a final study of the original material we are including Chart 2, which pictures the distribution curve based on deviation by per cent of actual from theoretical diameters. The smoothed curve was kindly developed from the rough figures by Mr. Harry Jones and his assistants in the Mathematical Department of the Mutual Benefit Life Insurance Company.

With the idea that it might be helpful in determining at a glance the approximate percentage deviation of the actual from the theoretical transverse diameter, we have added to Table II a separate table showing the plus and minus deviations from the theoretical given in column 1 of the table. For example, if it is determined that, for the height and weight given, the theoretical diameter is 120 mm. and the actual is found to be 150 mm., one can consult the special table, and find the number 120 in the column giving 0 per cent deviation. In this line the number 150 is found in the column indicating

plus 25 per cent. Accordingly, the applicant's transverse diameter is 25 per cent over the predicted. The percentage of deviation for any diameter which does not fall within the columns represented can be

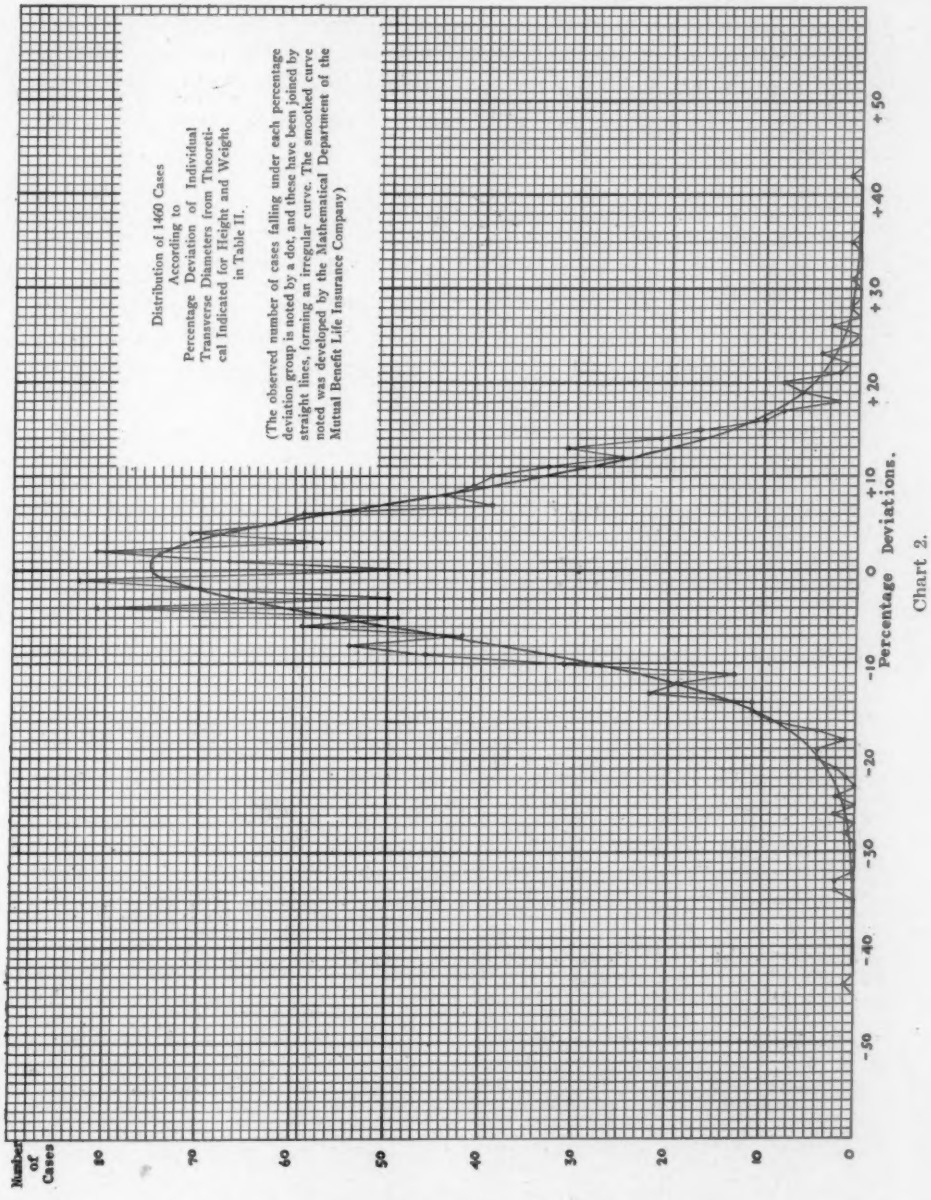

Chart 2.

approximated by reference to the two columns between which the observed falls.

It has generally been assumed that for the purpose of life insurance selection any heart diameter more than 10 per cent greater than the

average is to be regarded as indicative of hypertrophy of the heart. Pending future investigation of the actual effect on mortality of the deviation from average of the transverse diameter, it probably would be well in general to adhere to this figure. Nevertheless, we feel that judgment should be used in life insurance selection, since it is very certain that some hearts whose diameters are above 10 per cent of the expected are normal, just as others in which the heart diameter is distinctly less than the 10 per cent figure allowed are actually hypertrophied.

SUMMARY

A table was devised for obtaining the predicted transverse diameter of the heart silhouette based on the teleoroentgenogram.

The table is so constructed that it was found to be unnecessary to make any correction for excessive or subnormal height, or for age.

It would appear that when the systolic blood pressure is below 130 mm. the transverse diameter of the heart is normal. Above that level there is a slight or definite indication of increasing hypertrophy with increasing hypertension.

It is our opinion that, for the present, the predicted transverse diameter, plus 10 per cent, might be considered as the usual upper limit for the normal heart.

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Department of Clinical Reports

THE EARLY RISE OF BLOOD PRESSURE IN CORONARY THROMBOSIS*

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THE fall in blood pressure, both systolic and diastolic, which usually accompanies a coronary artery occlusion is one of the striking manifestations of the altered hemodynamics. This decrease in pressure is commonly mentioned as the most important of the criteria for differentiating it from an attack of angina pectoris, during which the blood pressure is frequently increased. While it has been observed that the pressure may not materially change during and after coronary occlusion, it is not sufficiently appreciated that the blood pressure may be higher than usual during the early painful phase of the attack. Thus, if a patient is seen in a prolonged attack of substernal pain with the blood pressure higher than it was when the patient was free of pain, a diagnosis of angina pectoris is often made and corresponding treatment administered.

A review of the literature reveals a paucity of observations as to the early rise of the blood pressure in coronary occlusion. Wood and Wolferth[1] anticipated the subject when they said: "The possibility presents itself that coronary occlusion produces an immediate rise of blood pressure in many cases, giving place to a subsequent fall at the time when these cases are usually seen by physicians. This explains the current belief that coronary occlusion and a drop in blood pressure are inseparable phenomena." They refer to a case of coronary occlusion reported by Fitz,[2] in which there was an accompanying rise of blood pressure. Barker[3] states that the blood pressure in coronary thrombosis usually falls considerably within a few hours, though a brief initial rise may be observed.

The following case reports of coronary occlusion are illustrative of the frequent observation that an increase in blood pressure may occur soon after the onset of the occlusion.

REPORT OF CASES

T. W., a white woman 64 years old, had known for fifteen years that she had high blood pressure. After a coronary occlusion in January, 1935, her blood pressure, which had been as high as 200/110, ranged between 160/90 and 180/100. On

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July 19, 1935, she was seen in an attack of coronary occlusion, the pain of which had lasted two hours. The blood pressure was 176/94. Despite opiates the pain gradually became worse, and one hour later the pressure was 190/110. The next morning she was free of pain and the pressure was 126/70. During the succeeding weeks it was as low as 90/60. In the following year the blood pressure ranged from 136/80 to 172/90. On July 22, 1936, she had another coronary occlusion. The pressure, half an hour after the onset of pain, was 146/92. The pain became very severe and the pressure rose to 170/100. Four hours later, when no pain was present, the pressure was 116/68. During the next sixteen months her blood pressure was as low as 86/56 and as high as 150/90. On Nov. 22, 1937, she had still another occlusion. When seen at the height of the pain, two hours after the onset, the pressure was 180/100. Three hours later she had no pain and the pressure was 100/60. Thirty minutes later she died suddenly.

M. A., a white man 58 years old, had known for one year that his blood pressure was high. For six months he had been having attacks of angina pectoris, which was the reason he came to the hospital. During the evening of the eighteenth day after entering the hospital he had a coronary occlusion. On the morning of the attack his blood pressure was 164/104. He was seen fifteen minutes after the onset of the painful features of the occlusion, at which time the pressure was 210/112. Five minutes later it was 230/120. One hour later the pain had been relieved and the pressure was 176/112. The next day it was 150/104, but two days later it was 112/66. Convalescence was uneventful.

J. S., a white man 45 years old, whose blood pressure had always been within normal limits, was hospitalized because of attacks of angina pectoris occurring at rest. Three days after admission to the hospital he had a coronary occlusion. The blood pressure the previous day was 126/80. He was seen one hour after the onset of the pain. The blood pressure was now 150/100. Thirty minutes later, when he was free of pain and was quiet, the pressure was 116/80. He made an uneventful recovery.

DISCUSSION

If the blood pressure increases as a result of coronary occlusion, it does so during the early painful stages of the attack. At this time the patient is restless, anxious, conscious of his suffering, possibly fearful of death. These mental aspects, along with the pain and oppression of the occlusion, probably initiate pressor reflexes which cause the rise of the pressure. Pain alone is not responsible, for I have seen patients who died in a state of anginosis with a rapidly falling blood pressure. It is also probable that a temporary compensatory increase in peripheral vascular resistance occurs at the onset of a coronary occlusion as it does in an attack of left ventricular failure or in shock, elements of both of which are usually present in a coronary occlusion. However, in none of the cases cited above and in the majority of other cases of coronary occlusion in which we have observed an early rise in pressure were there clinical signs of paroxysmal dyspnea, acute pulmonary stasis, or pulmonary hypertension. Fishberg[4] believes that shock or peripheral circulatory failure predominates in the first days of coronary thrombosis in individuals who have previously had slight or no symptoms of cardiac insufficiency. He comments on the observation that in the initial stage of traumatic shock the arterial pressure may rise, as a

consequence of arteriolar constriction in the extremities, before the fall. Mendlowitz, et al.,[5] found, in closed chest experiments following sudden ligation of the anterior descending branch of the left coronary artery in dogs, relatively insignificant immediate changes in the pressure. They thought this suggested that, for at least a short period following the coronary occlusion, a peripheral vasoconstriction occurred to compensate for the coincident diminution in cardiac output.

CONCLUSION

The blood pressure frequently rises during the early painful stages of coronary occlusion. This should not be confused with the increase in pressure which often accompanies an attack of angina pectoris.

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SPONTANEOUS RUPTURE OF A PAPILLARY MUSCLE OF THE HEART

Report of Case*

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THE spontaneous rupture of a papillary muscle of the heart is so rare that it has been referred to as a medical curiosity.[1] Many books on cardiology do not mention it. As pointed out by Stevenson and Turner,[2] there were two cases in 6,000 autopsies at the Baltimore City Hospital, none in 14,000 autopsies at the Johns Hopkins Hospital, and none in 2,000 autopsies at the University of Maryland Hospital. The present is the only case in 3,400 autopsies at the St. Louis University group of hospitals.

A review of the literature shows that only twenty-one cases have been reported. In 1935 Stevenson and Turner[2] reported one case and reviewed the literature up to that time. Nineteen cases had been reported and could be classified as follows: two cases of ruptured papillary muscle in the right ventricle, one case in which both papillary muscles in the left ventricle were broken, ten cases in which the left posterior papillary muscle was broken, and two cases in which the left anterior papillary muscle was broken; in four cases it was not stated which muscle was ruptured. In the case of Stevenson and Turner an anterior papillary muscle of the left ventricle was broken. In 1937 Payne and Hardy[3] reported a case of traumatic rupture of both papillary muscles in the left ventricle. Ours is another case of broken anterior papillary muscle of the left ventricle, the fourth to be published.

In most of the cases the rupture was caused by atherosclerosis of the coronary arteries with thrombosis and infarction of the myocardium. One resulted from syphilis,[4] one in the right ventricle from tuberculosis, another in the right ventricle from puerperal sepsis, and one from trauma.[3] Traumatic rupture of a papillary muscle is rather rare, although somewhat more frequent than spontaneous rupture. Some papers on traumas of the heart[5] do not include this condition.

The clinical picture in most of the cases is that of acute coronary thrombosis, and, when the muscle breaks, acute mitral insufficiency with pulmonary edema. In no case has the diagnosis of broken papillary muscle been made during life, but in the case of Wankel[6] the acute mitral insufficiency was recognized clinically. In our records there is a case in which the diagnosis of traumatic rupture of the chordae tendineae of

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the mitral valve was made by Dr. R. A. Kinsella about a year before death. The autopsy verified the diagnosis. The present discussion, however, is limited to rupture of the papillary muscles. In several cases a loud systolic murmur was heard at the apex of the heart, while in other cases it was a to-and-fro whistling murmur. In a few of the cases the patient stated that something had torn in his chest or heart. Most of the patients died suddenly, but a few survived for several months after the rupture.

Fig. 1.

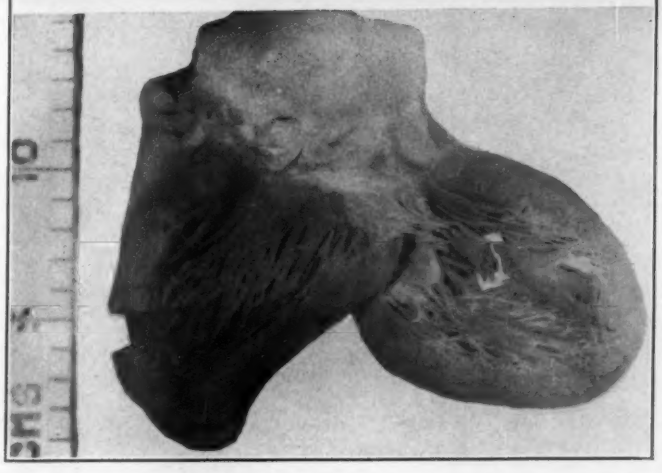

Fig. 2.

Fig. 1.—Broken anterior papillary muscle of the left ventricle. Fibrosis of myocardium.

Fig. 2.—Broken anterior papillary muscle of the left ventricle. Marked atherosclerosis of aorta.

CASE REPORT

A. S., a 52-year-old white man, had been known to have hypertension for at least ten years, the systolic blood pressure oscillating between 200 and 210. No signs of heart failure had been presented, nor had any murmurs been heard on ascultation.

The patient had drunk some beer the day before his death. On the day of his death he lapsed suddenly into unconsciousness after lunch and was seized with convulsions. When he recovered consciousness he complained of fullness in his chest,

Fig. 3.

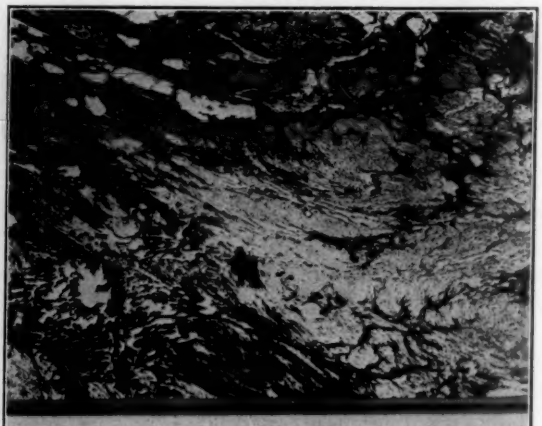

Fig. 4.

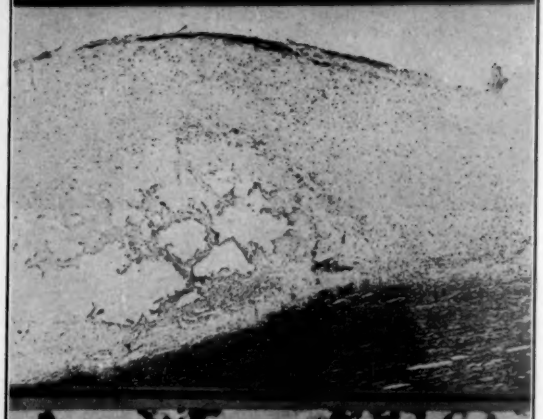

Fig. 5.

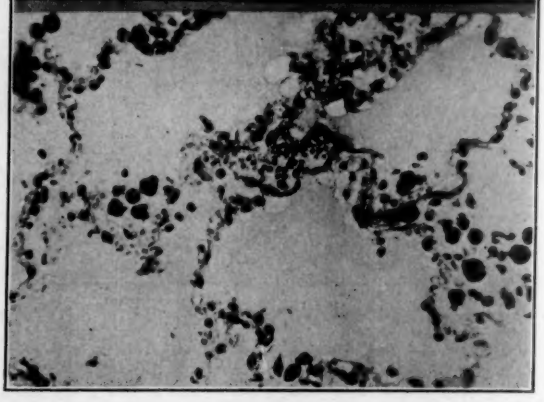

Fig. 3.—Marked fibrosis and necrosis of myocardium (Mallory stain).
Fig. 4.—Extreme atherosclerosis of aorta (hematoxylin and eosin).
Fig. 5.—Edema of the lungs, alveoli filled up with albuminous fluid, many heart-failure cells.

mainly in the precordial region. He remarked that his lungs were filling up and that he could not breathe. He was taken to the hospital, but died on the way.

Autopsy Findings.—The body was that of a well-developed and well-nourished white man approximately 50 years of age. The lips were markedly cyanotic. The jugular veins were very prominent and much engorged. The chest was broad and symmetrical. A very slight degree of edema was present over the ankles and the inner aspects of both thighs. There were about 50 c.c. of a thin, yellowish fluid in the right pleural cavity.

The heart was moderately enlarged, mainly due to enlargement of the left ventricle. The epicardium was quite smooth, thin, and intact. On examination of the heart before dissection, a soft area was found on the anterior wall of the left ventricle. On cut section this soft area was pale and thin, and was surrounded by an area of marked fibrosis. The anterior papillary muscle of the left ventricle was broken at a point about two-thirds of the distance from its origin to the point of insertion of the chordae tendineae. The torn edges were ragged and necrotic (Fig. 1). The base of this papillary muscle was in the center of the softened area mentioned above. The leaflet of the mitral valve normally attached to this muscle was freely movable in both directions and the valve must have been markedly incompetent. There was a marked degree of atherosclerosis in the proximal part of the aorta, mainly around the coronary openings (Fig. 2). The coronary arteries were tortuous, thick, and sclerotic; the anterior descending branch of the left coronary was completely occluded by an organizing thrombus.

The lungs showed an extreme degree of edema, were distended, and were heavier than normal. On cut section a large amount of serous, frothy fluid oozed from the parenchyma and the bronchi. Hypostatic congestion was also present. Both lungs were markedly anthracotic. The remaining viscera showed nothing but edema and congestion.

Microscopic Examination.—Sections of the heart taken from the infarcted area showed marked fragmentation and segmentation of the muscle fibers with some necrosis, lack of striation, pronounced fibrosis, and some areas of hemorrhage. The intima of the coronary vessels was markedly thickened with fibrous tissue. The aorta showed extreme thickening of the intima with fibrous tissue and deposits of lipoid material (Fig. 4). The media showed some edema, necrosis, and infiltration with lymphocytes and monocytes. The lungs presented very marked edema, an albuminous fluid filling most of the alveoli. There was also considerable congestion throughout the section, with many pigment-loaded phagocytes (heart-failure cells) (Fig. 5). A moderate amount of anthracotic pigment was present.

DISCUSSION

The interpretation of this case is rather simple. The sequence was: atherosclerosis of the coronary arteries with thrombosis of the descending branch of the left coronary, infarction of the anterior wall of the left ventricle, spontaneous rupture of the anterior papillary muscle of the left ventricle causing sudden insufficiency of the mitral valve, and acute pulmonary edema.

The cause of this acute pulmonary edema, we believe, is mechanical, and is due to the acute mitral insufficiency. Prior to this there had undoubtedly been weakening of the left ventricular muscle due to the infarction of the anterior wall of the ventricle.

It is well known that acute pulmonary edema can be produced experimentally in dogs and rabbits by ligating the aorta, by necrotizing the wall

of the left ventricle (with alcohol or 5 per cent silver nitrate), or by ligating three-fourths of the pulmonary veins.[7, 8]

Our case was one of sudden failure of the mitral valve and necrosis of the wall of the left ventricle.

Of the previously published cases, only in that of Wankel did acute pulmonary edema develop. It is an interesting fact that in Wankel's case it was also the anterior papillary muscle of the left ventricle which ruptured.

SUMMARY

This is the report of a case of very marked atherosclerosis of the coronary arteries, thrombosis of the anterior descending branch of the left coronary, infarction of the myocardium in the anterior wall of the left ventricle, spontaneous rupture of the left anterior papillary muscle, acute pulmonary edema, and sudden death.

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ARTERIAL THROMBOSIS FOLLOWING SIMPLE CONTUSION*

Report of a Case

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IN A clinic devoted to the study of vascular disease, the major portion of cases of thrombosis and embolism are secondary to disease of the heart or peripheral arteries in older persons. It is well known, of course, that arterial thrombosis may occur following trauma, but actual experience, as a rule, does not disclose many cases of this type. Arterial thrombosis following fracture of an extremity, and deep wounds which necessitate ligation of one or more large vessels are seen from time to time, but thrombosis resulting from a simple contusion is of sufficient rarity and interest to be worth recording.

The case of this type to be presented is instructive both from the standpoints of diagnosis and of treatment, for the history furnished evidence that thrombosis following a minor accident may be easily overlooked, and an unusual opportunity was offered to observe and evaluate the results of treatment in a young, healthy patient whose circulatory system was normal except for that portion of it affected by the injury.

CASE REPORT

The patient, a white boy, aged 16 years, reported to the Vascular Clinic of St. Luke's Hospital on Feb. 5, 1938. His complaint was that he had had pain in the right leg for six months, that is, since August, 1937. At that time, while acting as a caddy, he had been struck in the right calf by a golf ball. The ball had been driven from the preceding tee, and had struck him a direct blow; it had traveled about a hundred yards in the air before striking him. After the accident he was able to continue with his work throughout the day and, except for local pain and tenderness, experienced no unusual symptoms. The skin was not broken, but for a period of a week there was a definite area of ecchymosis.

Several days following the accident he noticed that it was difficult for him to walk without resting. He observed that his right leg tired more easily than the left, and after walking moderate distances he would frequently have slight pain in the right calf. It was always his observation that this pain was relieved by rest. He also had noticed that the right leg was usually colder than the left, and frequently appeared paler. In spite of the pain in the leg he was able to carry on his work as a caddy during the remainder of the golf season.

About two months after the accident his condition became much worse. He was able to walk only three or four blocks at a slow pace before the pain in the right leg developed. From November, 1937, until the time of his admission to the Clinic, there had been a gradual decrease in the distance he could walk until finally pain appeared after walking only about one block. He was attending school and found it impossible to participate in any athletic competition. At no time had he experienced pain when at rest.

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In the period of six months that had elapsed since the accident, during which the symptoms had become increasingly severe, the patient had consulted several physicians who had offered various diagnoses, such as arthritis, neuritis, and rheumatism, and had prescribed aspirin and other treatment without the slightest effect. No investigation of circulatory function had been made by anyone.

Except for the injury and its sequelae, nothing in the patient's past history was pertinent to the condition from which he sought relief. He had never had scarlet fever or diphtheria, his feet had never been exposed to cold weather, there was no history or evidence of diabetes, and he did not smoke.

A general physical examination and special examinations of the eyes, ears, nose, and throat showed no abnormalities, and all of the peripheral reflexes were normal.

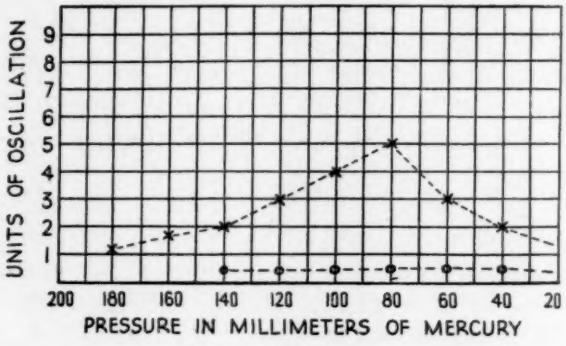

Fig. 1.—Oscillometric readings in both legs before treatment. (*X*, left leg; *O*, right leg.)

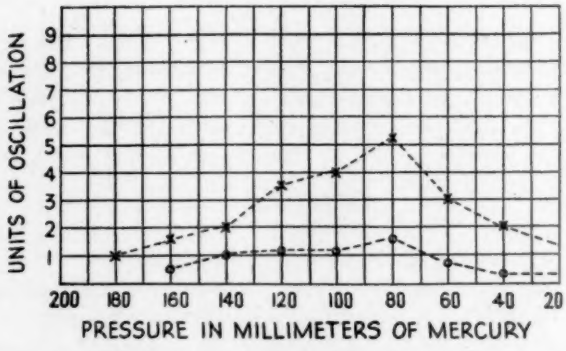

Fig. 2.—Oscillometric readings in both legs after passive vascular exercise (pavaex) treatment for sixty-five hours. (*X*, left leg; *O*, right leg.)

The patient was 5 feet, 6 inches tall, weighed 135 pounds, and appeared well developed and well nourished. The blood pressure was 110/70, and the pulse rate 72. Routine examinations of the blood and urine yielded normal findings, and the blood Wassermann reaction was negative.

Examination of the lower extremities revealed slight atrophy of the right calf muscles. Actual measurements indicated a difference of 3 cm. in circumference between the right and left legs. The right leg appeared to be paler than the left, in the horizontal position. On elevation, both feet and legs appeared pale. The pallor of the left leg was less marked than that of the right. In the dependent position the right leg showed a marked rubor, whereas the left leg was of a normal pink color. After exposure to room conditions the temperature of the right great

toe was 28° C. and of the left great toe, 32° C. There were no localized areas of tenderness. The femoral pulsations on both sides were normal. The popliteal, posterior tibial, and dorsalis pedis pulses were absent on the right side, but of good quality on the left. There was no edema, ulceration, or varicose veins. Oscillometric studies indicated good pulsation in both thighs. The pulse of the left leg and foot was normal, and the pulse of the right leg and foot was greatly diminished (Fig. 1). Intracutaneous histamine tests indicated a normal capillary response in both legs.

From the history and physical findings it was apparent that the patient was suffering from thrombosis of the posterior tibial artery, which probably was secondary to the injury suffered six months previously. Passive vascular exercise (pavaex) was instituted in an effort to establish an increase in the collateral circulation. From February 7 until June 4 the patient received this treatment for a total of sixty-five hours. No other form of treatment was administered during this period. The treatment was applied from one and one-half to two hours at a time, three times a week. More intensive therapy was not possible because the patient wished to remain in school.

During this period considerable subjective improvement was noted. The walking distance gradually increased and the degree of pain was considerably less. After the sixty-five hours of treatment the patient could walk about seven blocks without pain, as contrasted with one block when he was first examined. Improvement in the circulation was shown objectively, also, for the oscillometer recorded an increase from one-half to one and one-half units (Fig. 2). The temperature of the right foot was still lower than that of the left, but this was not noticeable to the patient. The temperature of the right great toe had risen from 28° C. to 30° C.

COMMENT

In many cases of thrombosis and embolism of the peripheral arterial system there is evidence that adequate collateral circulation develops spontaneously. For this reason it is often difficult to decide whether the treatment instituted early in the course of the circulatory disturbance is really responsible for improvement. In this instance, however, adequate time had elapsed since the occurrence of the injury to allow collateral circulation to increase spontaneously, if it were going to do so. Since, instead of any improvement, the patient's condition had become progressively worse before he presented himself at the clinic, and since after treatment was instituted he displayed marked betterment, it seems justifiable to conclude, in this case, that the passive vascular exercise (pavaex) treatment was responsible for the increase in circulation in the extremity.

During the summer vacation it will be possible for the patient to report more often for treatments, which are to be continued at least until they have been administered for a minimum of 100 hours. It is expected, in view of the patient's initial response, that additional improvement will result with continuation of this therapy.

AURICULAR FLUTTER AND COMPLETE HEART BLOCK

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WHEREAS auricular flutter and complete heart block are individually comparatively common, an association of the two conditions is unusual. The first accurate description of a combination of these disturbances in rhythm, with electrocardiographic proof, was reported by Jolly and Ritchie,[1] in 1911. Recently, Jourdonais and Mosenthal[2] described a case and thoroughly reviewed the literature; they found twenty-nine authentic cases, including their own. The details of these cases can be found in this article,[2] hence it is unnecessary to recapitulate them. The rarity of the condition is further emphasized by the fact that Willius[3] encountered it only once in the electrocardiograms of 40,000 patients, while at Kings County Hospital it has been observed only twice in over 20,000 records. The following report, which adds two more to the reported cases, gives a summary of the findings in these two cases.

REPORT OF CASES

Case 1.—M. R., a white man, 61 years of age, was admitted to Kings County Hospital for the first time on Nov. 1, 1935, complaining of shortness of breath, pain in the chest on exertion, cough, and swelling of the legs, all of seven months' duration; these symptoms had become more severe four weeks before admission. Neither his past nor family history was significant. Physical examination showed a large, well-nourished white man, sitting up in bed, orthopneic and cyanotic. The neck veins were distended as far as the angle of the jaw. The pulse was irregular, and the rate was 100 beats per minute. The blood pressure was 150/90. The vessels revealed a moderate degree of sclerosis. The apex beat was located outside the midclavicular line, 13 cm. from the midsternal line. There was a loud, blowing systolic murmur at the apex and a short rough systolic at the aortic area. Moist râles were heard at the bases of both lungs posteriorly. The edge of the liver was palpable three fingerbreadths below the costal margin and there was evidence of a small amount of free fluid in the abdominal cavity. The extremities showed slight edema. The blood sugar was 330 mg. per 100 c.c. A teleoroentgenogram of the chest showed a marked increase in the transverse diameter of the heart; the cardiothoracic index was 0.65. The electrocardiogram revealed auricular flutter at a rate of 250, with a varying block producing a ventricular rate of 100 (Fig. 1 *A*). Digitalis was ineffective in changing the rhythm but slowed the ventricular rate to about 60 beats per minute. The patient was discharged two weeks later, greatly improved; his diabetes was controlled without using insulin. The diagnosis was arteriosclerotic heart disease, and auricular flutter.

The patient was admitted to the hospital for the second time on June 23, 1936, having attended the cardiac clinic from time to time. Although digitalis was prescribed by the clinic physicians, he took it only occasionally—approximately one tablet a day for a few weeks and none for several weeks at a time. For at least

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two weeks before admission he had taken no digitalis or any other drug. On admission he had essentially the same complaints as previously, namely, dyspnea, precordial pain on exertion, and swelling of the legs and abdomen. The most important physical findings were orthopnea, cyanosis, distention of the neck veins, and rapid venous pulsations at the base of the neck. The blood pressure was 180/110. The pulse was slow (40 per minute) and regular.

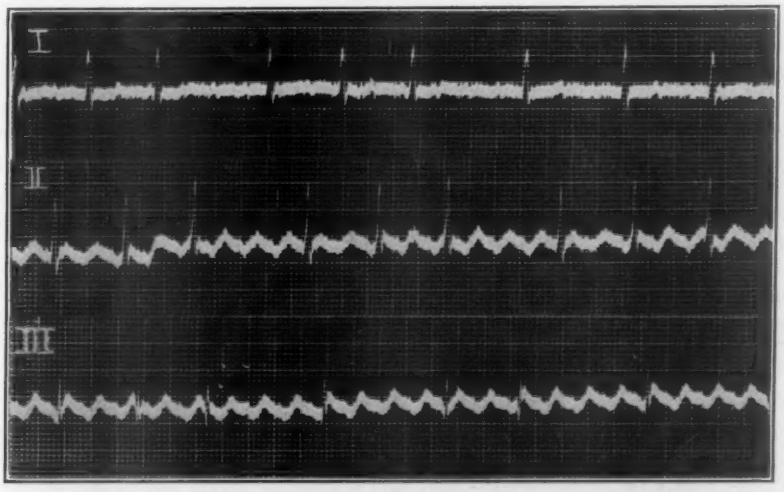

Fig. 1*A*.—Case 1. Auricular flutter with irregularity of the ventricle (Nov. 16, 1935).

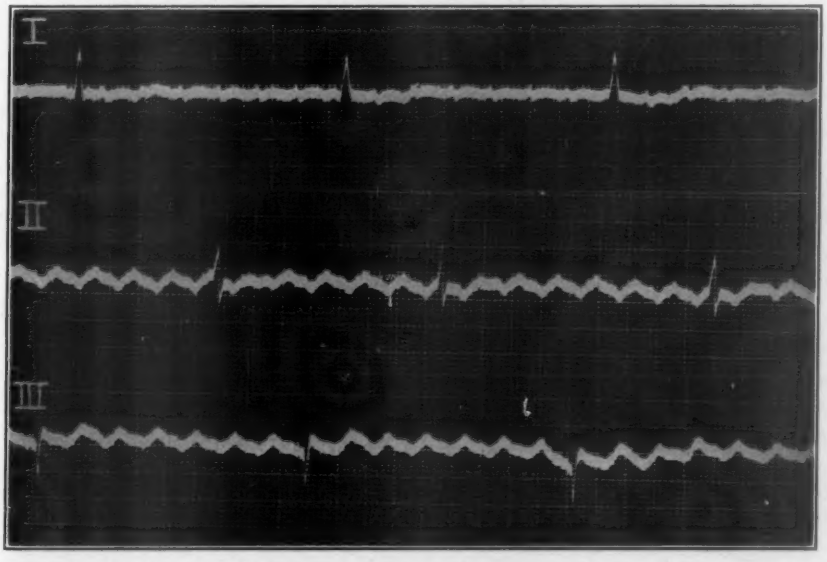

Fig. 1*B*.—Case 1. Auricular flutter with complete heart block (June 26, 1936).

The cardiac findings were the same as on the previous admission. There were moist râles at the bases of both lungs, enlargement of the liver, ascites, and edema of the legs. The electrocardiogram revealed auricular flutter at a rate of 214 and complete heart block with a ventricular rate of 33 (Fig. 1 *B*). He was again com-

pletely digitalized, and large doses of quinidine sulfate were given; both, however, were ineffective in changing either the rate or the rhythm.

Subsequently, he was readmited to the hospital three times before his death in November, 1937. On each occasion he had essentially the same complaints and physical findings and a heart rate which varied between 30 and 40. The anasarca was most resistant to any form of treatment, including complete digitalization, ammonium chloride, and mercupurin; both intravenously and in the form of suppositories. Numerous electrocardiograms all showed auricular flutter and complete auriculoventricular block.

CASE 2.—C. E., a white man, 62 years old, was admitted to Kings County Hospital on March 23, 1936, complaining of precordial pain and dyspnea. The family and past personal histories contributed nothing of significance. The patient was well until ten days before admission, when, while walking, he was seized with sudden severe substernal pain which caused him to fall to the ground and become dyspneic. Thereafter, he had had attacks of substernal pain on the slightest exertion.

Physical examination showed a white man lying quietly in bed, in no apparent discomfort. The important physical findings were a rapid regular pulse of 110, and a blood pressure of 140/100. The heart was slightly enlarged, the apex being situated just outside the midclavicular line. There were a few moist râles at the

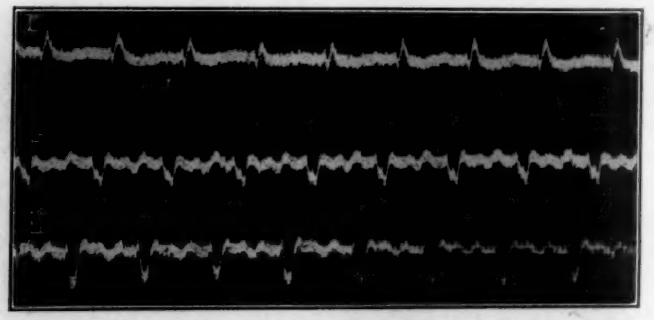

Fig. 2A.—Case 2. Sinus rhythm with intraventricular conduction disturbance and left axis deviation (March 25, 1936).

bases of the lungs. The laboratory data were negative. The electrocardiogram showed normal sinus rhythm at a rate of 110, left axis deviation, and intraventricular conduction disturbance (Fig. 2 *A*). A question which arises with respect to this record is whether the rhythm is normal sinus rhythm or auricular flutter. Leads II and III suggest the latter possibility, but on close analysis the timing of the peaks of the different waves does not appear to conform to that seen in auricular flutter. One concludes, therefore, that the rhythm is of sinus origin. Although the tracing does not show the typical features of acute coronary occlusion, in view of the history and the fact that there is a pronounced disturbance of intraventricular conduction (which frequently masks the characteristic findings of coronary thrombosis) a diagnosis of coronary occlusion was made. The patient was discharged from the hospital considerably improved, and directed to take 1½ grains of digitalis per day.

He remained well until September, 1936, when he was readmitted, complaining of shortness of breath on exertion and swelling of the legs and abdomen, of two weeks' duration. Physical examination showed an acutely ill individual, orthopneic and cyanotic, with distended neck veins. The pulse rate was slow (24 per minute) and regular, and the blood pressure was 180/100. The heart was tremendously enlarged, the apex being in the anterior axilliary line; the heart sounds were distant. Moist râles were heard at the bases of both lungs, and the liver extended three

fingerbreadths below the costal margin. Ascites and edema of the extremities were present. Except for a trace of albumin in the urine the laboratory findings were normal. The electrocardiogram (Fig. 2 *B*) showed auricular flutter at a rate of 214, complete heart block with a ventricular rate of 33, left axis deviation, and left bundle branch block. During the first few days in the hospital repeated Stokes-Adams attacks occurred; they were controlled by ephedrine and gradually disappeared. The patient was discharged at the end of three months in good condition, with no ascites or edema. The diagnosis was hypertensive and arteriosclerotic heart disease, auricular flutter, and complete heart block.

He re-entered the hospital in February, 1937, with practically the same complaints and physical findings as on the previous admission. The electrocardiogram again showed auricular flutter at a rate of 231, complete heart block with a ventricular rate of 30, left axis deviation, and an intraventricular conduction disturbance. He grew worse progressively, and died three days after admission.

On post-mortem examination the classical features of heart failure, including pulmonary edema, hydrothorax, ascites, and anasarca, were found. The heart

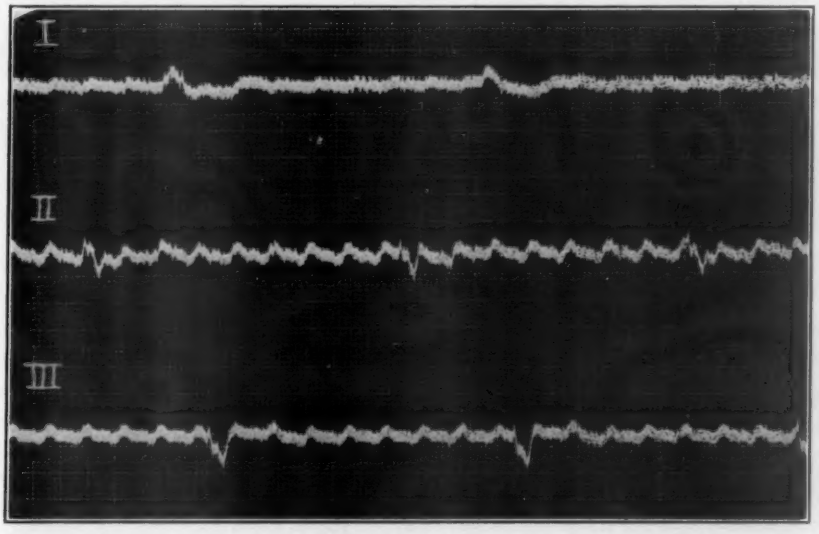

Fig. 2*B*.—Case 2. Auricular flutter, complete heart block, and left bundle branch block (Oct. 1, 1936).

weighed 800 gm.; the valves appeared normal and the main branches of the coronary arteries were patent. The myocardium showed a small amount of interstitial fibrosis and at the upper end of the interventricular septum there was an area of fibrosis measuring about 1 cm. in diameter. This undoubtedly was an old healed myocardial infarct involving the bundle of His, as had been suspected when he first came to the hospital.

DISCUSSION

The rarity of the association of auricular flutter and complete heart block has been alluded to already. Of the reported cases only four of the thirty-one, including the two reported in this paper, occurred in women. The age incidence varied from 13 to 74 years, with 80 per cent occurring in patients more than 50 years of age. This is to be expected, as a study of the etiology reveals that the condition takes place almost

exclusively in patients suffering from arteriosclerosis, hypertension, and coronary artery disease. There were only three cases of syphilitic heart disease, and one each of rheumatic, congenital, and thyreotoxic heart disease. Jourdonais and Mosenthal[2] have classified the previous cases into different groups, i.e., those in which the combination developed after the administration of drugs but in which one or the other disturbance of rhythm was present before medication was given, and those in which auricular flutter and heart block occurred spontaneously. In the majority of cases the disturbances appear spontaneously, but in a patient who is receiving digitalis, the possibility that it may be the cause must be seriously considered and the drug withdrawn in the hope that the abnormal rhythm will disappear. Neither of our patients had complete heart block when first seen, and in only one was auricular flutter present. Each received digitalis, and it might be thought that this was the cause of the block. In both instances, however, after complete block had supervened, digitalis was discontinued for considerable periods of time; nevertheless, the block persisted. Thus it seems more probable that the cause was progressive organic damage due to coronary artery disease. Indeed, in the second case, at post mortem, an area of fibrosis in the region of the main branch of the bundle of His was found. In the cases previously reported, quinidine sulfate stopped the flutter in five instances out of twenty-five, digitalis in two, and thyroidectomy in the only case of thyreotoxic heart disease. In the present series both patients received digitalis and one quinidine, but the abnormal rhythm persisted. The prognosis in the presence of the associated conditions is grave; one of our patients lived for six months and the other for seventeen months after the combination of rhythm disorders appeared. Signs and symptoms of right- and left-sided heart failure were present in each instance. The condition can be suspected clinically by observing the occurrence of rapid auricular pulsations in the jugular veins in a patient with a regular ventricular rate between 30 and 40. The diagnosis, however, can be made with certainty only by means of the electrocardiogram.

SUMMARY

Two cases of auricular flutter with complete heart block are reported. In both, the cause appeared to be coronary artery disease, and in neither were the abnormal rhythms affected by therapy.

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Department of Reviews and Abstracts

Selected Abstracts

Cossio, Pedro: Acoustic Phenomena of the Mitral Valves. Rev. argent. de cardiol. 4: 383, 1938.

The graphic registration of the heart sounds, together with other manifestations of the heart action in 40 cases of mitral stenosis (with and without auricular fibrillation), has shown that very often extra sounds occur in these cases early in diastole: opening snap of the mitral valve, reduplications of the second sound, or an especial sound towards the end of the rapid ventricular inflow. They explain the three and even four sounds often heard in mitral stenosis.

The opening snap occurs more frequently in older patients with predominant signs of stenosis. The rapid ventricular inflow sound occurs more likely in children and adolescents with recent rheumatic aggression and with predominant insufficiency of the mitral valve. The latter may be an ordinary third heart sound with a new acoustic element added, the result of the sudden tension of the diseased valve, caused by the distention of the ventricular wall. Sometimes it may be entirely due to this valvular tension, justifying the name of "tension snap" of the mitral valve.

The phonocardiograms nearly always show a diastolic murmur due to the stenosis and a systolic murmur due to the insufficiency of the valve. Sometimes only one of them is heard, and one gets the wrong impression that only one condition exists. The diastolic murmur begins a short interval after the second sound and shows two reinforcements: protodiastolic and presystolic. Both are fused together when the rapid ventricular inflow and the auricular systole fall together on account of tachycardia. Occasionally the diastolic murmur begins a short interval after the opening of the auriculoventricular valves, and this is interpreted on the assumption that the stenosis is not very great; consequently the conditions to produce the murmur arise only when the ventricular cavity reaches a certain volume. The presystolic murmur may be absent after long diastoles because of the inability of the auricle to inject blood in an overdistended ventricle.

The systolic murmur has variable characteristics and duration. It may be proto- meso- or holo-systolic according to the extent of the lesion or to the moment of its evolution. The following scheme may be drawn for the acoustic phenomena in cases of rheumatic disease of the mitral valve:

a. If the stenosis is slight and recent there is a proto- and meso-systolic murmur which predominates over the diastolic one, the latter even being inaudible; in the records the diastolic murmur may begin after the sound occurring during the rapid ventricular inflow.

b. If the stenosis is frank and older, there is a holo-systolic murmur, and the diastolic one starts either with the ventricular inflow, after the opening snap, or towards the end of that period, following the third sound above mentioned.

c. If the stenosis is marked and very old, there is a proto-systolic murmur masked by the first heart sound, and the diastolic murmur begins after the opening snap, nearly always present.

AUTHOR.

Heymans, Corneille: Experimental Arterial Hypertension. New Eng. J. Med. 219: 154, 1938.

The methods of producing hypertension experimentally are reviewed. The four methods described are as follows:

1. Section of the cardio-aortic and carotid sinus moderator nerves. Hypertension occurs here by the release of vasoconstrictor and cardioaccelerator centers, the activity of which, under normal conditions, is permanently moderated reflexly by the cardio-aortic and carotid sinus nerves.

2. Injection of a kaolin suspension into the cerebral ventricles or into the subarachnoid space. The mechanical compression thus produced leads to cerebral anoxemia, which particularly sensitizes the vasopressor centers to the stimulating action of carbon dioxide.

3. The production of renal ischemia through permanent, incomplete compression of the renal artery. It is suggested that the arterial hypertension induced by renal ischemia may be due to a humoral factor which increases the excitability of the peripheral blood vessels to constrictor stimulations, mainly to the neurogenic vasoconstrictor influences. The same humoral factor induces, on the other hand, a direct peripheral vasoconstriction and a disturbance in the physiologic mechanisms of the pressoreceptive reflex regulation of blood pressure.

4. Repeated large doses of vitamin D_2 (Calciferol) in dogs produces a progressive augmentation of the arterial blood pressure with the development in the kidneys, and elsewhere, of certain vascular lesions, mainly "arteriolonecrosis."

NAIDE.

Wilson, C., and Pickering, G. W.: Acute Arterial Lesions in Rabbits With Experimental Renal Hypertension. Clin. Sc. 3: 343, 1938.

Acute arterial lesions structurally identical with those of malignant hypertension in man have been found in rabbits with arterial hypertension produced by renal artery constriction. The incidence of the lesions was related to the degree of hypertension but not to its duration. These lesions were most frequent and severe in the intestine, but were also found in stomach, liver, suprarenal, heart, and eye; they were absent from the kidney, the renal artery to which had been constricted. It is suggested that a greatly raised intra-arterial pressure is a chief factor in determining these lesions in human and experimental hypertension.

HINES.

Moore, L. A., Hallman, E. T., and Sholl, L. B.: Cardiovascular and Other Lesions in Calves Fed Diets Low in Magnesium. Arch. Path. 26: 820, 1938.

Calves fed rations low in magnesium to the extent that the blood magnesium was reduced to a low level exhibited a definite pathologic picture. The principal pathologic alteration consisted of a deposition of calcium salts in the yellow elastic fibers of the endocardium, of the aorta, jugular vein and larger arteries, of the surfaces of the diaphragm and of the trabeculae and capsule of the spleen. Also notable were degeneration and calcification of Purkinje fibers. There were present also various degrees of hepatitis and nephritis. A possible relationship of diets low in magnesium to the arteriosclerosis of human beings is suggested.

AUTHORS.

Roth, Grace M., Maclay, Elizabeth V., and Allen, Edgar V.: Blood in Thromboangiitis Obliterans. Arch. Int. Med. 62: 413, 1938.

The values for serum calcium, serum protein, blood urea, serum lecithin and serum phosphorus were found to be within normal limits in a study of the blood in cases of thromboangiitis obliterans. In most instances the blood volume, hematocrit value and concentration of fatty acids and cholesterol in the plasma were found to be normal. In some instances the blood volume was slightly decreased, and the hematocrit value and the concentration of fatty acids and cholesterol in the plasma were slightly increased. The significance of these findings is doubted, since they are inconstant findings in thromboangiitis obliterans.

AUTHORS.

Stanojevic, L.: Determination of Circulation Time With Lobelin. Ztschr. f. Kreislaufforsch. 30: 521, 1938.

By using intravenous Lobelin (0.03 to 0.07 mg./kv.) the author determined circulation time objectively, since this drug produced coughing. The determination is simple and without risk. It can be repeated safely several times a day or after a few hours without signs of intolerance cumulation or toxicity. If desired, this can be recorded graphically with a pneumograph. It operates apparently on the cough center since the circulation time is of the order obtained with other methods, viz., on the average 10.6 seconds in normal subjects, 12.8 seconds in noncardiac patients, 13.4 seconds in cardiac patients without congestive failure and 30.2 seconds in congestive failure.

KATZ.

Korth, C.: Frontiers of Clinical Electrocardiography. Arch. f. Kreislaufforsch. 3: 1, 1938.

The recent advances in clinical interpretation of the electrocardiogram are evaluated in view of recent work. It was found that inverted T-waves are more significant when in Leads I or I and II than when in Lead III. Abrupt changes in direction of T are particularly significant. In infectious diseases, the T-wave contour is important in estimating myocardial damage. The S-T segment has gained greater meaning clinically within recent years. The value of electrical systole in tetany is stressed. Considerable value is to be attached also to the axis deviation.

KATZ.

Rühl, A.: The Significance of Severe Anoxic Variations of the T Wave in Healthy Subjects. Ztschr. f. Kreislaufforsch. 30: 393, 1938.

The electrocardiographic variations were noted on placing normal subjects in a low pressure chamber and lowering the atmospheric pressure to the equivalent of altitudes of from 16,250 to 21,125 feet. A total of 118 observations were made. It was found that T was flattened in Leads I and II and S-T was depressed in these leads. Exercise before subjecting the individual to the high altitudes increased the deviation of S-T and T.

KATZ.

Schlomka, G., and Dietrich, H.: Physiological Arhythmia of the Heart. VI. In Emphysema. Ztschr. f. Kreislaufforsch. 30: 453, 1938.

One hundred patients were studied. The results are opposed to the view that the sinus arrhythmia is not caused by a central radiation of impulses from the

respiratory to the cardioregulatory centers. The sinus arrhythmia increases in degree at first as the lung involvement increases and then with further lung involvement tends to decrease.

KATZ.

Walter, R.: Correlation Between Pulse Frequency and Conduction Time as a Sign of Myocarditis. Ztschr. f. Kreislaufforsch. **30**: 481, 1938.

A prolonged P-R interval is an early sign in myocardial inflammation. This is accompanied by tachycardia. Tachycardias such as follow exertion in normal individuals differ from the tachycardias in damage to the heart muscle in that the former are unaccompanied by prolongation of P-R. However, even in myocarditis, tachycardia following exertion is not associated with prolongation of P-R.

KATZ.

Schlomka, G., and von Königslöw, E.: The Evaluation of the Relative Duration of Systole. IV. Extrasystoles. Ztschr. f. Kreislaufforsch. **30**: 487, 1938.

When correlated with the duration of the preceding diastole, the systole of the postextrasystolic beat following a compensatory pause was found to be relatively longer than the other sinus beats. This was less noticeable following supraventricular extrasystoles than following ventricular ones. This relative prolongation of systole is also less marked in diseased hearts than in normal ones.

KATZ.

Langendorf, R., and Pick, A.: Electrocardiogram in Acute Nephritis (two parts). Acta Med. Scandinav. **94**: 1, 1938.

This is a report on twelve cases of acute diffuse glomerular nephritis. A flattening or inversion of T was found in Lead I, with a bifid T-wave in some cases, and in Lead III (and II) T became large and upright. In Lead IV, T became inverted (new terminology) and sometimes T became bifid. The absence of S-T deviations and Q-wave changes distinguish this condition from coronary occlusion with myocardial infarction. The discordancy of changes in Leads I and III and the absence of S-T changes distinguish this type from that in pericarditis.

In the evolution of the changes, the T-wave in Lead I becomes inverted and T_3 becomes typically peaked, and Lead IV develops a deep T, resembling superficially the changes in anterior myocardial infarction. The author attributes changes to heart strain on the left side which is caused by the sudden hypertension, but this is not the sole cause as some ischemic, toxic, or other effects on the myocardium must play a rôle.

KATZ.

Winternitz, M., and Langendorf, R.: The Electrocardiogram in Pericarditis. Acta Med. Scandinav. **94**: 141, 274, 1938.

This is a report of 76 cases of pericarditis including 8 of traumatic origin with hemopericardium, 18 of rheumatic origin, 14 of tuberculous origin, 12 of uremic origin, 2 due to blastomatosis, 11 of a septic nature, 5 following myocardial infarction, and 5 of unknown origin. These cases are critically reviewed and correlated with the literature on the subject. Characteristic changes occurred in 46 cases, no change in 15, and noncharacteristic abnormalities in the rest. Most characteristic early in the disease is the presence of an elevated S-T segment concave upward followed by an upright T-wave. The terminal portion of QRS is pulled upward. These early changes last for about three days, when S-T deviations disappear and T

becomes flatter. Later T becomes inverted, but the T-wave and S-T evolution are not coordinated in time. Also, before becoming inverted, T may be split, or appear as a late, small deflection. Later T becomes a characteristic coronary type and waxes and wanes. Precordial leads are not characteristic of the lesion but fail to show the typical coronary occlusion evolution. The cause for electrocardiographic changes is not due to ischemia of muscle or tamponade or to subepicardial myocardial damage, but the authors consider them due to bioelectric changes in the tissues surrounding the heart. The negative T-wave, however, is due to an action in the heart.

KATZ.

Master, Arthur M., Dack, Simon, and Jaffe, Harry L.: Partial and Complete Heart Block in Acute Coronary Artery Occlusion. Am. J. M. Sc. **196**: 513, 1938.

A complete review has been made of the A-V conduction disturbances in 375 cases of coronary artery occlusion with reference to their incidence, clinical, electrocardiographic and pathologic features, prognosis and treatment.

Simple P-R prolongation was common, occurring in 16 per cent of cases; partial and complete heart block occurred in 3.2 per cent.

Heart block appeared soon after the onset of the occlusion and usually lasted one to two weeks. P-R prolongation not infrequently appeared late and became permanent.

Permanent P-R prolongation and heart block may be the result of previous unrecognized coronary occlusion. Repeated attacks of occlusion may progressively increase the A-V conduction defect.

The sudden onset of P-R prolongation as well as heart block may be the first and only sign of coronary artery occlusion.

Heart block, excluding P-R prolongation, was associated with heart failure, cardiac enlargement, previous hypertension, and previous coronary occlusion. It was more common in older patients with advanced arteriosclerosis.

Symptoms attributable to the heart block appeared only when the ventricular rate fell to 40 or less and consisted of heart failure or the Stokes-Adams syndrome with syncope and coma. The bradycardia can differentiate the latter from syncope and coma due to other causes, such as shock and cerebral embolus.

The prognosis of complete heart block was serious, because of the slow ventricular rate. Four of the six patients died. Partial heart block offered a favorable prognosis unless there was marked bradycardia. Simple P-R prolongation did not affect the outcome of an attack adversely.

It was confirmed that complete and partial heart block were associated with a specific cardiac lesion and electrocardiographic pattern. The anatomic basis was infarction of the posterior portion of the interventricular septum and posterior surface of the left ventricle as a result of right coronary artery occlusion. The electrocardiogram presented the Q-3 T-3 pattern typical of posterior wall infarction.

The presence of profuse anastomotic channels in the interventricular septum around the A-V node prevents the more frequent occurrence of heart block and affects its remission when it does occur.

P-R prolongation was not associated with a specific anatomic lesion or electrocardiographic pattern. Anoxemia, heart failure, and vagal influences were probably significant.

The association of A-V block with intraventricular block can be attributed to septal infarction which involves simultaneously the A-V tissues and bundle-branch system.

The treatment of heart block is that of coronary artery occlusion in general. When there are persistent bradycardia and Stokes-Adams manifestations, adrenalin

should be resorted to. The indications and effects of adrenalin, ephedrine, and atropine are discussed. Digitalis, quinidine, and nitroglycerine were considered contraindicated.

AUTHOR.

Hadorn, W.: Combined Thrombo-Emboli of the Coronary Arteries. Ztschr. f. Kreislaufforsch. **30**: 563, 1938.

An unusual case is reported where a thrombus over a myocardial infarction gave rise to an embolus which lodged in the same coronary artery in which an earlier thrombus had resulted in the infarction. This coronary embolus caused sudden death of the patient.

KATZ.

Hines, E. A., Jr., and Roth, Grace M.: The Effect of Tobacco on the Blood Pressure as Measured by a Standard Smoking Test. Proc. Staff Meet., Mayo Clin. **13**: 524, 1938.

A standard smoking test and a control test have been carried out on fifty-six patients with essential hypertension and thirty subjects with normal blood pressure. Cigarette smoke produced an elevation of blood pressure in the majority of individuals tested by a standard smoking test. The excessive rises in blood pressure from smoking occurred only in the patients who had evidence of an inherently hyperreactive vascular system as measured by the cold pressor test. The effect of smoking tobacco on the blood pressure, however, is not due entirely to a nonspecific stimulus acting on a hyperreactive vascular system but is the result, at least in part, of some element in the tobacco smoke which produces vasoconstriction.

AUTHORS.

Alam, M., and Smirk, F. H.: Blood Pressure Raising Reflexes in Health, Essential Hypertension, and Renal Hypertension. Clin. Sc. **3**: 259, 1938.

A study has been made of the effects of blood pressure raising reflexes in normal subjects, patients with essential hypertension, and patients with renal hypertension. Two different methods of testing the blood pressure raising reflexes were employed: (1) the stimulus of exercising the forearm muscles during arrest of the circulation as previously described by the authors; (2) a modification of the cold pressor test as described by Hines and Brown. Effects on the blood pressure were similar with both tests. It was found that the effects on the systolic blood pressure are greater in old than in young subjects but there was no difference in the effect of age on the diastolic pressure. The rise in both systolic and diastolic pressures is less in patients with renal hypertension than in normal subjects of the same age group. Large effects are more frequent in cases of essential hypertension than in normal controls of the same age. Large rises of blood pressure may occur in normal subjects and small rises in patients with essential hypertension. No definite correlation was found between a high degree of reactivity and the resting blood pressure level. In the majority of cases of essential hypertension the natural relationship between the pulse rate and blood pressure is reversed in that a rise in blood pressure is accompanied by a rise in pulse rate.

HINES.

Barker, Nelson W.: Lesions of Peripheral Nerves in Thromboangiitis Obliterans. Arch. Int. Med. **62**: 271, 1938.

In a histopathologic study of the peripheral nerves in a series of twenty cases of thromboangiitis obliterans various combinations of wallerian degeneration, fibrosis,

edema, atrophy, lymphocytic infiltration, inflammation and thrombosis of the vasa vasorum were noted in all but one case. A definite correlation was found between the presence of wallerian degeneration and the clinical syndrome of ischemic neuritis. The presence of these degenerative changes proximal to the site of nerve section or alcohol injection explains the failure to relieve pain with these procedures.

NAIDE.

Saleeby, Eli R., and McCarthy, Patrick A.: Aneurysms. Pennsylvania M. J. 41: 969, 1938.

Thoracic and abdominal aneurysms can be prevented by early and intelligent treatment of syphilis.

The Matas obliterative endoaneurysmorrhaphy offers the best available means of cure for external aneurysms.

The present treatment of internal aneurysms is unsatisfactory.

The Babcock procedure of end-to-end anastomosis of the common carotid artery and internal jugular vein offers the best available means of alleviating the symptoms of intrathoracic and subclavian aneurysms untreatable by other means.

There have been no instances of rupture of an intrathoracic aneurysm following the Babcock procedure.

AUTHOR.

Cleland, J. B.: Periarteritis Nodosa; Report of Two New Cases. M. J. Australia 1: 847, 1938.

There seems to be a definite relationship between periarteritis nodosa and rheumatic fever, and it is possible that the former disease is in some cases an allergic response to the agent of rheumatic fever. Three cases of periarteritis nodosa were found in 4,000 autopsy cases in two Australian hospitals. One of these three cases presented rheumatic vegetations on the mitral valve. Allusion is made to previous cases with associated rheumatic manifestations. The cause of periarteritis nodosa, of course, has not been proved.

MONTGOMERY.

Fatherree, T. J., and Hines, E. A., Jr.: Fatal Complications of Thrombo-Angiitis Obliterans: A Clinical Study. Proc. Staff Meet., Mayo Clin. 13: 342, 1938.

The cases are reported of twenty-two individuals with thromboangiitis obliterans who died, including nine on whom necropsy was performed. In sixteen cases, or 73 per cent of the group, extraperipheral vascular lesions played a dominant role as the cause of death. Four of these deaths followed operation. Coronary thrombosis is by far the most common type of peripheral lesion producing death in cases of thromboangiitis obliterans. In none of the post-mortem cases was a lesion found in the visceral arteries which was typical of the pathologic changes described by Buerger.

AUTHORS.

Lewis, Thomas: Raynaud's Disease and Preganglionic Sympathectomy. Clin. Sc. 3: 321, 1938.

Six unselected cases of Raynaud's disease have been examined shortly after preganglionic sympathectomy. Observation of these cases shows that preganglionic sympathectomy does not bring the fingers to a common state; it relieves in all cases, but a local abnormality remains, and this can be displayed in a measure that is re-

lated to the abnormality displayed before operation. The full vasodilatation resulting from preganglionic sympathectomy declines in a period of about a week following operation.

HINES.

Rosenberg, Edward F., Keith, Norman M., and Wagener, Henry P.: Diffuse Arterial Disease With Hypertension: Two Unusual Cases of Contrasting Types. Arch. Int. Med. 62: 461, 1938.

The term diffuse arterial disease when used in a broad sense includes cases in which there are primary changes both in the arteries and in the arterioles. Two contrasting cases are reported in which the preponderant alteration in one was in the arterioles, whereas in the other it was in the arteries.

In the first case, with arteriolar involvement, the retinal picture was characterized by diffuse edema of the retina and of the optic nerve, with various hemorrhagic and exudative lesions and with visible changes in the retinal blood vessels. In the second case, with sclerosis of the larger arteries, the retinal changes were minimal, consisting of mild arteriovenous compression and mild narrowing of the retinal arterioles; a slight change in the color of the arterioles was also present.

The general conclusion is drawn that in patients with sustained hypertension, the site of the predominating change, whether it is an abnormal physiologic process or an actual anatomic lesion, is in the arterioles; on the other hand, in patients with diffuse atherosclerosis of the arteries, hypertension is often mild and fluctuating or even absent.

NAIDE.

Clara, M.: Anatomy and Biology of the Blood Supply of the Kidney. Arch. f. Kreislaufforsch. 3: 42, 1938.

An excellent summary beautifully illustrated is presented of the architecture of the renal vascular supply based on the author's work correlated with that in the literature.

KATZ.

Bähr, E.: Atherosclerosis of the Coronary Arteries in Relation to Age, Disease and Constitution. Arch. f. Kreislaufforsch. 3: 95, 1938.

A study based on 308 autopsies of subjects from 4 months to 92 years of age is presented in which analysis of macroscopic changes in the major coronary vessels was made. A novel type of diagram was used to depict the distribution of atherosclerosis in the coronaries at various age groups. It was found that the left descending coronary is the one involved earliest and the one which is most intensely involved at all age groups. The left circumflex is least involved and the right circumflex is intermediary. Exceptions to this occur when the right coronary artery is unusually long or the right ventricle is hypertrophied. Atherosclerosis increases with increased work of the heart. The so-called white collar class and professional groups show more involvement of the coronaries than manual laborers. The florid and robust type of person has coronary sclerosis while the asthenic has this disease only on rare occasions.

KATZ.

Anthony, A. J., and Lent, W.: The Distensibility of the Vessels of the Extremities. III. Ztschr. f. Kreislaufforsch. 30: 528, 1938.

Curves of distensibility of the arteries of the extremities were obtained by correlating the pulse wave velocity with the "wirksam" internal pressure. Marked individual variations were obtained in young, healthy persons while the curves of old

persons were similar in shape. Little differences were seen in the average curve obtained from healthy young people, old people, and hypertensive patients. On the whole, the distensibility of the healthy subjects was greater at low pressures.

KATZ.

Grant, R. T., and Holling, H. E.: Further Observations on the Vascular Responses of the Human Limb to Body Warming; Evidence for Sympathetic Vasodilator Nerves in the Normal Subject. Clin. Sc. 3: 273, 1938.

Recent observations have revealed that while body warming provokes a large increase of blood flow and skin temperature in the hands and feet it causes no more than a slight rise in blood flow and skin temperature in the proximal part of the extremities, and neither flushing nor warming of the skin of the proximal portion occurs provided the circulation to the extremity is arrested. This variation has been explained as being due to the difference in the distribution of the arteriovenous anastomoses. The present study was carried out to see if further information could be obtained as to the reason for the difference in reactions. The subjects to be tested were subjected to strong body warming accomplished by immersing two or three extremities in water maintained at 45 to 46° C. and with other portions of the body completely covered except the face and the limb under observation. Blood flow and skin temperature were measured by methods previously described. It was found that when body warming was pushed to excess in this manner vasodilation develops in the proximal areas of the extremities. Observations were made in several patients before and after sympathetic ganglionectomy and on several subjects following nerve block. The results obtained from these and previous observations are interpreted as indicating two means of defense against rise in body temperature. The first is brought into action by relatively gentle heating and consists chiefly of a dilatation of the arteriovenous anastomoses in the extremities caused by the inhibition of vasoconstrictor tone. The second occurs when the heating is more intense and consists mainly of a general dilatation of the cutaneous vessels associated with sweating. The vasodilation produced in the proximal part of the extremity is brought about by stimulation of cutaneous sympathetic nerves.

HINES.

Stewart, Harold J., Deitrick, John E., Crane, Norman F., and Wheeler, Charles H.: Action of Digitalis in Uncompensated Heart Disease. Arch. Int. Med. 62: 561, 1938.

From the detailed study of the mechanism of the action of digitalis on the circulation of forty-two patients suffering from heart disease the following conclusions are drawn:

The output of blood per minute from the heart which is in failure is diminished, the velocity of the blood flow is less and the heart is larger than when it is in a state of compensation. The work per beat is decreased and is not commensurate with the size of the organ. The venous pressure is in certain instances elevated, and in others it is in the normal range.

Digitalis increases the output per minute of the failing heart, decreases its size and increases the work per beat, so that it more nearly approximates what is expected of it for its size. The circulating blood now moves at a greater velocity. A fall in venous pressure occurs if it was elevated beforehand.

An interpretation of these results in the light of those already reported is that digitalis has the same action on the normal as on the pathologic heart; it decreases the cardiac size, which is interpreted as an effect on tone. The amount of the cardiac output which results from this action depends on the initial size of the heart.

The amount decreases in the case of a normal heart and increases in the case of a dilated one. The evidence indicates that digitalis acts in a similar fashion on the normal heart and on those damaged by valvular disease and by myocardial disease unless the myocardial damage is extreme, in which case toxic effects might possibly be elicited at lower concentrations of digitalis.

The effect of digitalis in the presence of auricular fibrillation is similar to that recorded when the rhythm is regular.

The response of hearts damaged by syphilis, arteriosclerosis, and hypertension appears to be similar to that observed for hearts damaged by rheumatic fever.

The response of patients whose aortic valves are damaged is not different from that of patients exhibiting mitral involvement.

The decrease in cardiac size appears to be the most important effect of digitalis, the change in cardiac output being a consequence of it.

The lowering of the venous pressure by the administration of digitalis to the patient exhibiting heart failure seems to be dependent on an increase in cardiac output. An increase in cardiac output and work per beat permits the pumping onward of the blood accumulated on the right side so that a proper distribution results.

There are indications that digitalis may benefit certain patients with organic heart disease without heart failure (Christian), but the final proof will depend on clinical observations.

When considered in the light of data relating to the action of the drug when the heart is normal and to its action when the heart is damaged by organic heart disease but heart failure is not present, the observations now reported with respect to patients with failure, those presenting regular sinus rhythm as well as those exhibiting auricular fibrillation, lead the authors to restate their original conclusion. Digitalis has similar, perhaps identical, action when the heart is normal and when it is diseased. It decreases the cardiac size and increases the extent of ventricular contraction, and to these is to be added the effect on systolic tension. The consequence of these actions is that the cardiac output which results differs, depending on the initial difference in the size of the ventricular cavities in the two situations. In the one (the normal heart and the diseased heart which is not failing) it becomes too small; in the other (the diseased heart which is failing) it acquires a suitable size.

These studies demonstrate, however, a more uniform generalization which is applicable to all these situations, namely, that digitalis increases the work of the heart per beat and that with respect to the heart which is failing, it increases the work per beat and makes it more nearly commensurate with the work expected of the heart for its size.

AUTHORS.

Stewart, Harold J., Crane, Norman P., Deitrick, John E., and Thompson, W. P.: Action of Digitalis in Compensated Heart Disease. Arch. Int. Med. 62: 547, 1938.

The authors gave 1.6 to 1.8 gm. of digitalis within twenty-four hours to thirteen patients suffering from rheumatic heart disease and to four others with arteriosclerotic, hypertensive or syphilitic heart disease. In all cases there was compensation, and a normal sinus mechanism was exhibited. In addition to clinical studies of these patients, special observations were made of the cardiac output, cardiac size, circulation time, and venous pressure. In all cases the T-wave and the R-T segment of the electrocardiogram showed the changes characteristic of a digitalis effect. It was found that seven patients showed a decrease in cardiac output and a decrease in cardiac size, four patients showed an increase in cardiac output and a decrease in cardiac size, and six patients showed no change in cardiac output and in cardiac

size. In short, in some instances when the heart was made smaller, the cardiac output increased, and in others it decreased. In the former cases the heart behaved like a failing heart, and in the latter cases like a normal one. They were unable to predict beforehand which effect would be produced.

The results in five patients exhibiting auricular fibrillation were not different from those encountered in those with normal sinus rhythm—a decrease in cardiac size was associated with a decrease in cardiac output, and an unchanged cardiac size was associated with an unchanged cardiac output.

Digitalis has four effects on the heart which may be recorded clinically: (1) an effect on contraction, namely, an increase; (2) an effect on size, namely, a decrease; (3) an effect on the cardiac rate, namely, a decrease; and (4) an effect on the electrocardiogram, indicating an effect on the cardiac muscle. The cardiac output which results is different, depending on the individual heart, that is to say, whether it is dilated or not.

A few observations on patients with heart disease due to other etiological factors showed that these phenomena are not confined to those with rheumatic involvement.

There is one phenomenon which is common to all groups: The giving of digitalis increases the work accomplished by the heart per beat, whether its action is to increase or to decrease the ouput or to leave it unaltered and whether the rhythm is regular or is that of auricular fibrillation. As a consequence, work becomes more nearly appropriate for the size of the organ. Some basis is afforded Christian's suggestion of giving digitalis to the patient suffering from organic heart disease even though he shows no significant failure.

These studies yield additional evidence that a decrease in cardiac output which follows the giving of digitalis to human beings (normal and those having organic heart disease without congestive heart failure) is not a consequence of diminished venous return but a consequence, so far as we can now ascertain, of a decrease in the size of the heart due to the action of digitalis on it.

AUTHORS.

Von Storch, Theodore J. C.: Complications Following the Use of Ergotamine Tartrate. J. A. M. A. 111: 293, 1938.

Analysis of all the reports of serious sequelae following the use of ergotamine tartrate reveals that the great majority of the complications arose because of overdosage, pre-existing sepsis, or obliterative vascular disease. Twenty-one of the total of forty-two patients reported in the literature developed gangrene. No accidents have been reported following its use in the migraine syndrome.

Treatment, by the author, of 189 patients with migraine headaches over a period of five years has resulted in no serious complications.

Contraindications to the use of ergotamine tartrate are sepsis and obliterative vascular disease, including disease of the coronary arteries. Caution should be used in the presence of marked arteriosclerosis, hepatic or renal disease, vitamin C deficiency, and hypersensitivity to the drug.

When correctly administered and attention is paid to warning symptoms ergotamine tartrate may be considered a safe and valuable method for the treatment of migraine headaches.

NAIDE.

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THE American Heart Association, sponsor of the first International Health Broadcast, stands alone as the national organization devoted to educational work relating to diseases of the heart. Its Board of Directors is composed of twenty-five physicians representing every portion of the country.

The Section for the Study of the Peripheral Circulation was organized in 1935 for the purpose of stimulating interest in investigation of all types of diseases of the blood and lymph vessels and of problems concerning circulation of blood and lymph. Any physician or investigator in good standing may become a member of the section after election to the American Heart Association and payment of dues to that organization.

To coordinate and distribute pertinent information, a central office is maintained, and from it issues an ever widening stream of books, pamphlets, charts, posters, films, and slides. These activities all concern the recognition, prevention or treatment of the leading cause of death in the United States, diseases of the heart. The AMERICAN HEART JOURNAL is under the editorial supervision of the Association.

The income from membership and donations provides the sole support of the Association. Lack of adequate funds seriously hampers more widespread educational and research work imperative at this time. Great progress has been made, but much remains to be done.

Annual membership is $5.00 a year and journal membership at $10.00 includes a year's subscription (January-December) to the AMERICAN HEART JOURNAL and annual membership in this Association. A cordial invitation to join in this crusade is extended to you.

The American Heart Association solicits your support to the end that it may continue more effectively the campaign to which it has devoted all its energy.

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